"COMPARISON OF POSTOPERATIVE ANALGESIA AFTER INTRATHECAL NALBUPHINE WITH LEVOBUPIVACAINE AND FENTANYL WITH LEVOBUPIVACAINE AFTER GYNAECOLOGICAL SURGERY"

Dissertation submitted to

THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY

in partial fulfillment for the award of the degree of

DOCTOR IN MEDICINE

IN

ANAESTHESIOLOGY

BRANCH-X

INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE

MADRAS MEDICAL COLLEGE

CHENNAI - 600 003.

MAY - 2019

CERTIFICATE

This is to certify that the dissertation entitled, "**COMPARISON OF POSTOPERATIVE ANALGESIA AFTER INTRATHECAL NALBUPHINE WITH LEVOBUPIVACAINE AND FENTANYL WITH LEVOBUPIVACAINE AFTER GYNAECOLOGICAL SURGERY**" submitted by **Dr.A.SUGANYA.,** in partial fulfilment for the award of the degree of Doctor of Medicine in Anaesthesiology by The Tamil Nadu Dr.M.G.R. Medical University, Chennai is a bonafide record of the work done by her in the INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE, Madras Medical College and Government Hospital, during the academic year 2016-2019.

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DECLARATION

I hereby, solemly declare that this dissertation entitled, **"COMPARISON OF POSTOPERATIVE ANALGESIA AFTER INTRATHECAL NALBUPHINE WITH LEVOBUPIVACAINE AND FENTANYL WITH LEVOBUPIVACAINE AFTER GYNAECOLOGICAL SURGERY"** is a bonafide record of the work done by me in the Institute of Anesthesiology and Critical Care, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, during the academic year 2016-2019 under the guidance of **DR.B.CHANDRIKA M.D.D.A,** Professor of Anaesthesiology, Institute of Anaesthesiology and Critical Care, Madras Medical College, Chennai-03,and submitted to The Tamil Nadu Dr.M.G.R.Medical University,Guindy,Chennai-32,in partial fulfilment for the requirements for the award of the degree of M.D.Anaesthesiology (Branch X),examinations to be held on May 2019.

I have not submitted this dissertation previously to any university for the award of degree or diploma

Place: Chennai **DR.A.SUGANYA.**

Date:

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CONTENTS

INTRODUCTION

INTRODUCTION

Spinal anaesthesia has a rapid onset and complete motor blockade and also simple to perform. It has lower incidence of failed block and the local anaesthetic requirement is less. Hence spinal anesthesia is a preferred anaesthetic technique for lower abdominal surgeries.

Adjuvants to local anaesthetics for intrathecal administration has some advantages. They have synergistic action &intensify sensory block without increasing sympathetic block, reduced local anaesthetic drug dose, better hemodynamic stability with lesser side effects.

Fentanyl is pure mu receptor agonist .It is lipophilic with rapid onset of action following intrathecal administration. The intrathecal drug concentration does not produce respiratory depression. It improves anaesthetic quality without much complications. The common mu agonist side effects are nausea, vomiting, sedation, urinary retention and respiratory depression.

Nalbuphine is a mixed kappa agonist and mu antagonist opioid drug, which produces analgesia without much side effects of mu receptor agonistic action.

Levobupivacaine is a local anaesthetic amide which can produce better sensory and motor block with good hemodynamic profile than bupivacaine. Levobupivacaine can cause lesser cardiotoxicity than bupivacaine.

Many investigators have studied the characteristics of intrathecal nalbuphine & fentanyl with levobupivacaine.

The purpose of this study is to compare the intrathecal fentanyl & nalbuphine as an adjuvant to levobupivacaine during gynaecological surgery for postoperative analgesia.

AIM OF THE STUDY

AIM OF THE STUDY

To compare post operative analgesic efficacy of intrathecal nalbuphine with levobupivacaine vs intrathecal fentanyl with levobupivacaine

Secondary Objectives:

A. Assessment of onset of sensory and motor blockade

B. To assess intra operative and postoperative hemodynamics

C. To evaluate the effective analgesic time

D. To evaluate the severity of pain using visual analog scale

E. Complication rate

REVIEW OF LITERATURE

REVIEW OF LITERATURE

❖ HALA MOSTAFA GOMAA ET AL[1]

They did a study in “comparison of the analgesic efficacy between intrathecal nalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine in patients undergoing cesarean section”.They selected 60 patients and divided them into

Group A with 30 patients who received intrathecal fentanyl 25microgram with 0.5% heavy bupivacaine and

Group B with 30 patients who received intra thecal nalbuphine 0.4mg with 0.5%heavy bupivacaine.

They monitored intraoperative and postoperative vitals like Heart rate, blood pressure and oxygen saturation. They assessed the onset of sensory and complete motor blockade, time of sensory blockade, duration of analgesia and motor blockade and adverse effects.post operatively visual analog scale score was used to asses the pain .The effective analgesic time was noted. The patients with pain score >3 received rescue analgesia Injection paracetamol 1000mg i.v.the time for the first rescue analgesia was longer in nalbuphine group but the difference was insignificant. Adverse effects were less common in nalbuphine group than fentanyl group but the difference was insignificant. They also observed that there was nil significance between the two groups with respect to intra operative and post operative hemodynamic variables.

❖ **GANGANDEEP SINGH et al[10]**

They did a study on 80 pregnant women posted for elective cesarean section who were divided into group A for them intrathecal 0.5% levobupivacaine with fentanyl 25 microgram given and group B for them intrathecal 0.5% levobupivacaine given.

They evaluvated the time of onset of sensory blockade, time to complete sensory blockade and two segment regression time, time for rescue analgesia and hemodynamics were monitored. They observed that the combination of fentanyl with levobupivacaine has achieved earlier complete sensory and motor blockade than levobupivacaine alone group. Also levobupivacaine with fentanyl reduced the need of postoperative analgesics.

❖ **MUKHERJEE et al[14]**

They did a study on 100 patients undergoing elective lower limb orthopaedic surgery under subarachnoid block. They used different doses of intrathecal nalbuphine (200,400,800 micrograms) added to 0.5% hyperbaric bupivacaine for Group A,B, and C respectively. They assessed the onset time for sensory and complete motor blockade and effective analgesic time,2 segment regression time and hemodynamics of the patients. They concluded that the duration of sensory block and effective analgesia were prolonged with doses of 400microgram (group B) and 800 micrograms (group C) of nalbuphine with bupivacaine but higher doses of nalbuphine produced higher side effects

❖ **MISIRLIOGLU et al[33]**

They did a study among 72 patients undergoing elective cesarean section .Group L received intrathecal 0.5% levobupivacaine and fentanyl 25microgram .Group B received intrathecal 0.5% bupivacaine with fentanyl 25microgram.They assessed the time to achieve sensory block upto T6,time to S2 regression, sensory and motor blockades at the end of the surgery .Hemodynamic parameters and neonatal APGAR score were recorded. They found that the quality of sensory blockade was equal in both the groups, but group B had complete motor blockade at the beginning and end of the surgery. Hemodynamic and neonatal parameters were similar in both groups. Pruritis was a common side effect in both groups. They concluded that levobupivacaine with fentanyl has effective sensory blockade with less motor blockade and similar hemodynamics than bupivacaine with fentanyl.

❖ **JAIDEEP SINGH et al[7]**

They did a study in 60 patients posted for lower abdominal surgeries. Group B received intra thecal 0.5% bupivacaine 3ml with fentanyl 25 microgram and group N received intra thecal 0.5% bupivacaine with nalbuphine 0.8mg.The onset of sensory and motor block, duration of motor blockade, VAS score, hemodynamic and side effects were analysed. They concluded that complete motor block rapid with fentanyl than nalbuphine and effective analgesic time and postoperative analgesia more prolonged in

nalbuphine group which was insignificant. Side effects were less in nalbuphine group.

- **AJITKUMAR SINGH et al[8]**

They observed“ Intraoperative hemodynamic profile in patients undergoing lower limb and abdominal surgery under subarachnoid block using 0.5% hyperbaric levobupivacaine” in 60 patients who underwent elective surgery were taken .They assessed for the maximum onset of motor and sensory block, hemodynamic parameters after administration of intrathecal 0.5% levo bupivacaine 4ml in 30 patients and intrathecal 0.5% bupivacaine in 30 patients. They found that levobupivacaine has similar onset of action with bupivacaine but has better hemodynamic profile in spinal anaesthesia

- **TIWARI J.P et al[2]**

They conducted a study among 80 patients who underwent gynecological procedures under intra thecal 0.5% levobupivacaine 3ml with dexmeditomidine 5microgram (group D) and 0.5%levobupivacaine 3ml with 0.5ml normal saline(group S). They measured time of onset &maximum level of sensory blockade and intensity of motor block, duration of analgesia by VAS, side effects like hypotension, nausea ,vomiting, respiratory depression. In group D faster onset and intense blockade with lesser side effects observed than group S.Thus overall the combination of levobupivacaine with dexmeditomidine better over levobupivacaine alone

❖ **SUMAN CHATTERJEE et al[4]**

They did a study among 96 patients undergone infra umbilical surgeries.they divided them into 3 groups.

Group L received intrathecal 0.5% isobaric levobupivacaine 2.8ml with 0.4ml normal saline,

Group LB received intrathecal 0.5%levobupivacaine 2.8 ml with butorphanol 25microgram,

Group LN received 0.5% levobupivacaine 2.8 ml with nalbuphine 0.4mg.

The onset, level, duration and regression of motor and sensory block with duration of effective analgesia and hemodynamic parameters were recorded. The onset of sensory block was same in LB and LN group than group L but motor blockade was faster in Group LN .Effective analgesic time also prolonged in Group LN. Levobupivacaine with nalbuphine provided longer duration of blockade and more prolonged analgesia

❖ **SUNITHA JAIN et al[5]**

They did a study in "Comparative study of ropivacaine 0.5% plain versus levobupivacaine (0.5%)plain in gynecological surgeries" and published in International Journal of Reproduction, Contraception, Obstetrics and Gynecology in 2017 february.

60 patients underwent gynecological surgeries were assessed in this study. They were randomly divided into Group R –intrathecal 0.5%ropivacaine

3.5ml and Group L- intrathecal 0.5% levobupivacaine 3.5ml.They measured the hemodynamic parameters and onset of sensory and motor block. The onset was faster and longer duration of block noted in group L with levobupivacaine than ropivacaine. Group R with ropivacaine were hemodynamically better than levobupivacaine group L

- **XAVIER CULEBRAS et al[17]**

They performed a study in 2000 titled advantages of intrathecal nalbuphine over intrathecal morphine after cesarean section -an evaluation of postoperative analgesia .90 persons were included in this study .Patients received 0.5% hyperbaric bupivacaine with morphine 0.2mg (categoryA), nalbuphine 0.2mg(category B),nalbuphine 0.8mg (category C),nalbuphine 1.6mg(category D).They found that postoperative analgesia was longer with morphine than nalbuphine . Adverse effects like pruritis, nausea, vomiting were more in morphine group. APGAR scores similar in all groups. Among nalbuphine categories -nalbuphine 0.8mg with bupivacaine group has prolonged analgesia with lesser side effects

- **FOURNIER et al[15]**

They performed a study in 1998 regarding the onset and offset of intrathecal morphine versus nalbuphine for postoperative pain relief after total hip replacement. The objective was to compare the postoperative analgesia for which twenty four geriatric patients posted for elective total hip replacement

were randomized into two groups. Spinal anaesthesia was given with 0.5% hyperbaric bupivacaine and morphine 160microgram in group A and nalbuphine 400microgram in group B. Patients were monitored 24hrs then they concluded that intrathecal nalbuphine produces faster onset of sensory and motor blockade but shorter duration of analgesia than morphine group

- **JYOTHI B,SHRUTHI GOWDA et al[18]**

They did a study in 2014 titled "A comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopedic surgeries".100 patients were selected from both sexes under American society of anaesthesiologist physical status 1 and 2. They were randomly allocated into four groups.

Group 1-intrathecal 0.5%bupivacaine 15mg +0.5ml normal saline

Group 2-intrathecal 0.5%bupivacaine 15mg+0.8mg nalbuphine

Group 3- intrathecal 0.5% bupivacaine 15mg +1.6mg nalbuphine

Group 4-intrathecal 0.5%bupivacaine 15mg +2.5 mg nalbuphine

The time to two segment regression of sensory block significantly prolonged in nalbuphine groups. The postoperative pain scores reduced from group 2 to 4. They conclude that adding 0.8mg nalbuphine with 0.5%bupivacaine in spinal anaesthesia provides better analgesia with lesser side effects. Nalbuphine exhibits analgesic ceiling effect at 0.8mg dose, further increasing the dose didn't rise the efficacy of analgesia.

PHYSIOLOGY OF PAIN

PAIN PHYSIOLOGY

Pain can be defined as “unpleasant emotional or sensory experience associated with potential or actual tissue damage or described in terms of such damage”

The experience of pain involves a series of complex neurophysiologic processes, termed as nociception. It has four components:

transduction, transmission, modulation and perception

Preemptive analgesia is administration of analgesic before the surgical incision, which prevents the establishment of central sensitization resulting from incisional injury.

BIOLOGICAL RESPONSE TO TISSUE INJURY

Physiologic consequences of noxious stimuli

Metabolic:

- Hyperglycemia
- lipolysis
- Protein catabolism
- hypermetabolism

Cardiovascular effects:

- Increased heart rate
- Increased cardiac output
- Increased blood pressure

Respiratory effects:

- Decreased tidal volume
- Decreased Functional residual capacity
- *V/Q* mismatch
- Increased oxygen consumption
- Decreased cough
- Diaphragmatic splinting

Other systemic effects:

- Sodium and free water retention
- Hypercoagulability
- Increased fibrinolysis
- Decreased gut motility
- Gastric acid secretion
- Altered immune function and Cytokine production

PAIN PATHWAY:

At the injury site,the local inflammatory mediators produces noxious stimuli which sensitizes nociceptors and there will be hyperalgesia.

Most nociceptors are free nerve endings .They sense heat ,mechanical and chemical tissue damage.

A fast, sharp and well localized sensation is conducted by thin myelinated A delta fibres (tested by pin prick) which has 2-5 micron diameter and short latency (0.1s) with conduct rate-12to 30 m/sec.

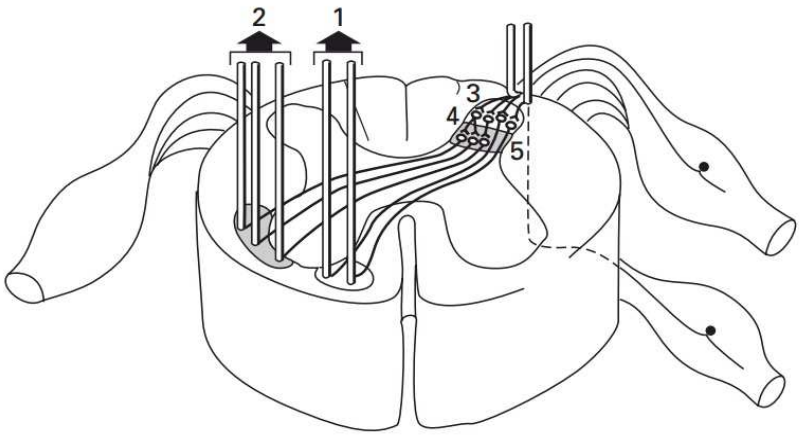
A slow onset, dull and poorly localized pain is conducted by unmyelinated C fibres which is 0.4 to 1.2micron diameter with conduct rate 0.5 to 2 m/s.

Type 1fibres including Abeta and some A delta fibres are high threshold Polymodal nociceptors which responds to extreme pressure and extremes of temperature (>42 degree celcious) and noxious substances such as histamine, prostaglandins, bradykinin, serotonin, Capsaicins

SPINAL CORD AND PROJECTIONS

THE DORSAL HORN:

The nociceptive impulses generated by peripheral nociceptors travel via the peripheral nerves, and the cell bodies of which are situated in the dorsal root ganglion. DORSAL HORN IS THE RELAY CENTER FOR NOCICEPTIVE IMPULSES.



Spinal nerve root and spinal cord: pain transmission. 1, 2: Spinothalamic and spinoreticular tracts. 3: Lissauer's tract, dorsal root entry zone. Note fibres ascending (they also descend) before entry. Note some fibres (12%) entering via ventral rather than dorsal root. 4: Dorsal horn, substantia gelatinosa (Rexed lamina 3). 5: Rexed laminae 4, 5, 6.

The spinal grey matter divided into 10 laminae on the basis of cytoarchitectonic studies. Laminae I–VI make up the dorsal horn, VII–IX forms ventral horn and lamina X is a cluster of cells around the central canal. Lamina I is named as marginal layer, lamina II the substantia gelatinosa and II–IV the nucleus proprius

ASCENDING SYSTEMS:

Nociceptive information is transmitted from the dorsal horn to thalamus and the higher centres via the lateral and ventral spinothalamic tracts.

The main nociceptive pathway is the spinothalamic tract. The cell bodies of the which are situated in the dorsal horn in laminae I, V–VIII and IX and they cross within one to two segments and then ascends. They project to the hypothalamus, peri-aqueductal greymatter, reticular formation of the medulla, mid-brain, pons and to medial and intralaminar thalamic nuclei.

CEREBRAL PROCESSESING

Projections from the thalamus run to an area rich in opioid receptors, peri aqueductal greymatter to the somatosensory cortex in the post-central gyrus, then the frontal lobes and hypothalamus

DESCENDING SYSTEMS

The main neurotransmitters involved in descending pathways are serotonin (5-HT) and norepinephrine

Descending modulation is initiated in the peri-aqueductal greymatter (mainly), in the medial and lateral reticular formation, and in the nucleus raphe magnus then they travels via the pons to the dorsal horn of the spinal cord.

GATE CONTROL THEORY OF PAIN

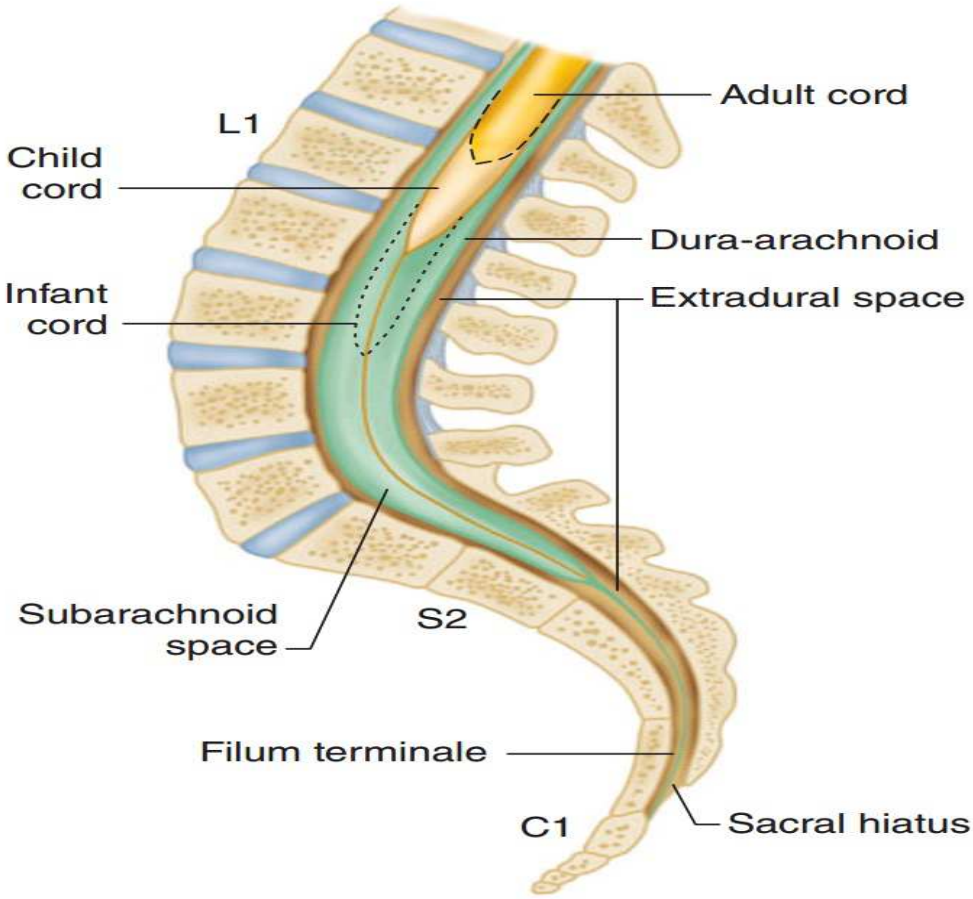
Gate control theory of pain modulation was given by Ronald Melzack and Patrick Wall in 1965. Usually the gate will be opened by nociceptive information which projects into supraspinal regions, but the gate close when flooding the dorsal horn with nonpainful stimuli(cutaneous touch or pressure) which stimulates Abeta fibres which are faster than Adelta and C fibres.

SPINAL ANAESTHESIA

SPINAL ANAESTHESIA

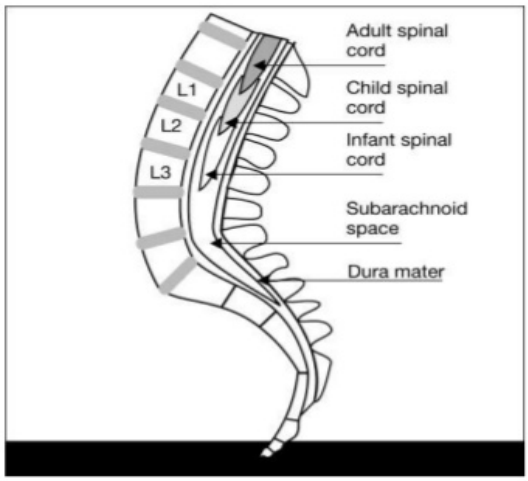
- Subarachnoid block was introduced by AUGUST BIER in 1898.
- Injection of local anaesthetics into the subarachnoid space usually at the lumbar level at L3-L4 to produce central neuraxial blockade at the nerve root level.

SAGGITAL VIEW OF LUMBAR SPINE



- Spinal canal contains spinal cord with three meningeal coverings (pia mater, arachnoid mater, duramater),venous plexus and fatty tissue
- Cerebrospinal fluid is present between pia and arachnoid maters in the subarachnoid space.
- Spinal cord extends cranially upto foramen magnum then continuous with brainstem, and caudally terminates in conus medullaris as the filum terminale (fibrous extension) and cauda equine (neural extension) at the level of upper border of L1 in adults and lower border of L3 in infants.
- The dural sac ,subarachnoid and subdural spaces extend upto S2 in adults and S3 in children.
- Filum terminale penetrates the dura and attaches conus medullaris to periosteum of the coccyx.

Termination of Spinal Cord

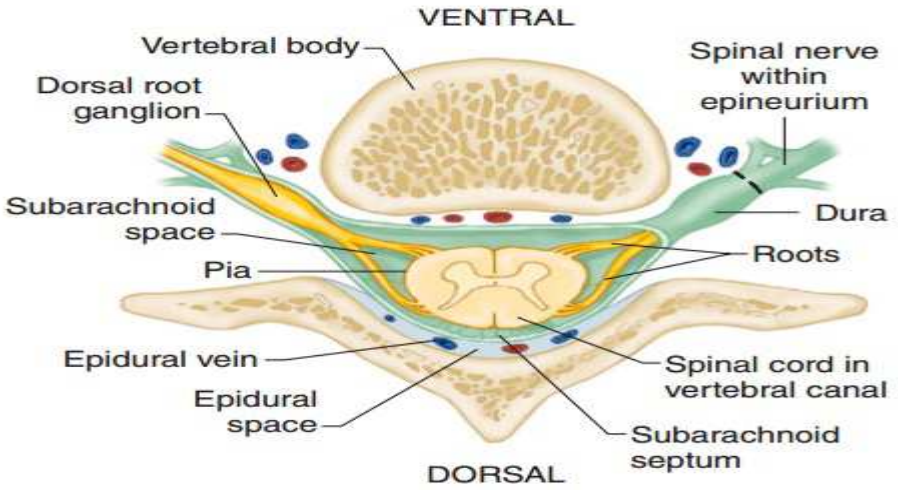


In adults usually ends at L1.

Infants L3

There are anatomical variations. For most adults it is generally safe to place a spinal needle below L2 unless there is a known anatomic variation.

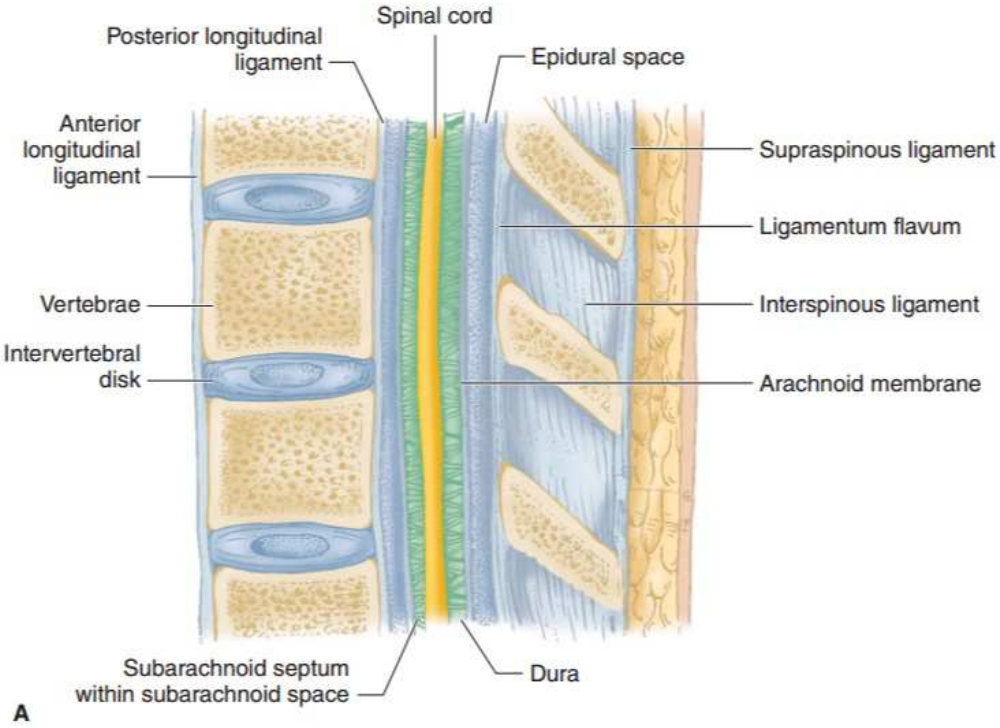
VIEW OF SPINAL CORD AND SPINAL NERVES



The anterior and posterior nerve roots at each spinal level joins and exit through the intervertebral foramina,from C1 to S5.

TUFFIER'S LINE- it is a line drawn between highest point of both iliac crests and it usually corresponds to L4 spine or L4-L5 interspace

STRUCTURES PIERCED IN SPINAL ANAESTHESIA



1.SKIN

2.SUBCUTANEOUS TISSUE

3.SUPRASPINOUS LIGAMENT

4.INTERSPINOUS LIGAMENT

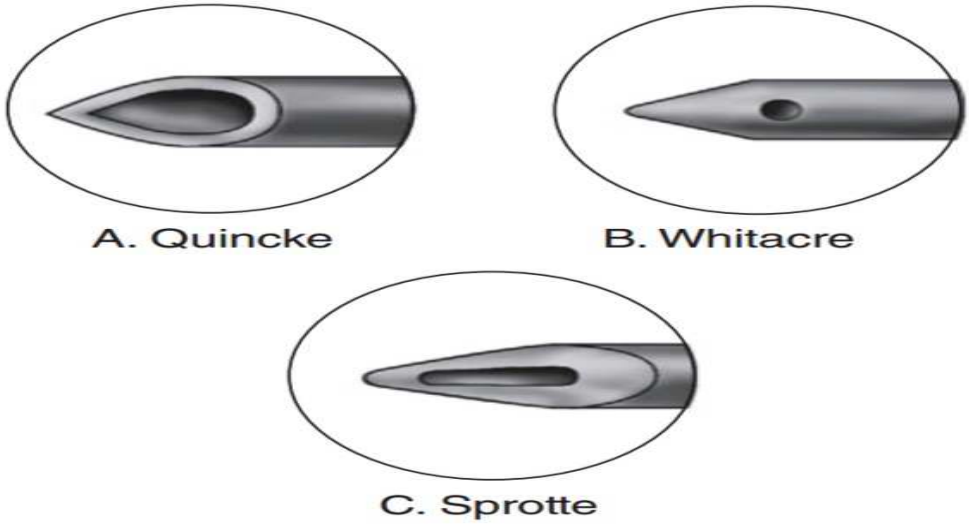
5.LIGAMENTUM FLAVUM

6.DURAMATER

7.ARACHNOID MATER

8.SUBARACHNOID SPACE

TYPES OF SPINAL NEEDLES



DURA CUTTING NEEDLES

It is associated with higher postdural puncture headache incidences

1.quincke-babcock

2.greene

DURA SEPERATING NEEDLES

It is associated with lesser postdural puncture headache incidence

1.whitacre

2.sprotte

3.pitkin

Spinal needles are available from 16 to 30 gauge sizes

DERMATOMAL LEVEL OF SPINAL SEGMENTS

C7-it is prominent and easily palpable SPINOUS PROCESS of C7 vertebrae

T4- at the level of Nipple

T6- at the level of Xiphi sternum

T7-Inferior angle of scapula

T10-at umbilicus

L1-Inguinal ligament

S1to S4- perineum

ADVANTAGES OF SPINAL ANAESTHESIA:

- Patient will be alert during the surgery
- Better pain relief
- Small dose and volume of the local anaesthetics can produce dense motor and sensory block
- Low incidence of postoperative nausea and vomiting
- Cost effective than general anaesthesia
- Sympathetic block produces vasodilation resulting in increased blood flow to the legs and decreased incidence of deep vein thrombosis

CONTRAINDICATIONS:

- ABSOLUTE-Patient refusal
- Coagulopathy or bleeding diathesis

- Increased intracranial tension
- Infection at the injection site
- Shock, severe hypovolemia
- Fixed cardiac output lesions like severe mitral and aortic stenosis, hypertrophic obstructive cardiomyopathy, complete heart block.
- Severe spinal deformity
- Preexisting neurological deficits /demyelinating lesions

POSITIONS IN SPINAL ANAESTHESIA

1.SITTING

2.LATERAL

3.PRONE POSITION

APPROACHES :

1. Midline- needle is inserted in midline with slightly cephalad direction.
2. Paramedian-needle inserted 1cm lateral and 1cm below the inferior aspect of spinous process
3. Taylor's approach-a type of paramedian approach, needle is directed in L5-S1 space ,1cm medial and 1cm inferior to posterior superior iliac spine

FACTORS AFFECTING HEIGHT OF BLOCK

MODIFIABLE FACTORS:

Volume and concentration of the local anesthetic drug(dose)

Site of drug injection

Position of the patient

Baricity of the drug

NONMODIFIABLE FACTORS:

Volume and density of cerebrospinal fluid

Pregnancy and advanced age

FACTORS AFFECTING DURATION OF BLOCK

Dose of the drug

Pharmacokinetics of the drug like liphophilicity,protein binding

Adjuvants to the local anaesthetics

BARICITY OF DRUG

Baricity means specific gravity of the local anaesthetic solution in relation to CSF. It determines spread of local anaesthetic drug in subarachnoid space. The specific gravity of CSF-1.0069.

ORDER OF BLOCKADE:

1.preganglionic sympathetic B fibres

2.temperature (cold then warmth)

3.pinprick

4.pain greater than pin prick

5.touch sense

6.pressure sense

7.proprioception

8. motor nerves

ASSESSMENT OF MOTOR BLOCKADE:

MODIFIED BROMAGE SCALE:-

0-no motor block

1-Inability to raise extended leg,able to move knees and feet

2-Inability to raise extended leg and move knee but able to move feet

3-complete motor block of the limbs

COMPLICATIONS:

- Sympathetic block produces vasodilation leads to hypotension
- High spinal blockade
- Postdural puncture headache
- Local anaesthetic induced neurotoxicity
- Iatrogenic -Meningitis,arachnoiditis ,cauda equine syndrome,hematoma formation
- Backpain
- Transient neurological symptoms due to lignocaine

PHARMACOLOGY OF

DRUGS

PHARAMACOLOGY OF DRUGS

LOCAL ANAESTHETICS

They have one lipophilic group (aromatic benzene ring) and hydrophilic group(tertiary amine) and an intermediate chain includes an Ester or Amide linkage.

1884-KARL KOLLER first used cocaine for ocular anaesthesia

Local anaesthetics are classified on the basis of intermediate chain as esters or amides.

ESTERS	AMIDES
COCAINE	PRILOCAINE
PROCAINE	ARTICAINE
CHLORPROCAINE	MEPIVACAINE
TETRACAINE	LIGNOCAINE
	ETIDOCAINE
	BUPIVACAINE
	LEVOBUPIVACAINE
	ROPIVACAINE

MECHANISM OF ACTION OF LOCAL ANAESTHETICS:

Local anaesthetics binds to voltage gated sodium channels

Reversibly inhibits conformational change of sodium channel

Blocks sodium influx into the cells

Prevents depolarization

Threshold potential not reached and action potential not propagated

(not alter the resting transmembrane potential in the nerves)

- Local anaesthetics are weak bases with pKa above the physiological pH.
- They are poorly soluble in water so prepared with hydrochloride salts for better stability
- Alkalinization of local anaesthetics shortens the onset of neuronal blockade and enhances the depth of sensory and motor block and improve the speed of blockade
- Adjuvants mixed with local anaesthetics prolong the duration of block

- Vasoconstrictor (epinephrine 1:200000) added to local anaesthetics limits the systemic absorption and maintains the drug concentration at nerve fibres resulting prolonged block

ADVERSE EFFECTS:

- Allergic reaactions produced by para amino benzoic acid which is a metabolic product of ester local anaesthetics or methylparaben preservatives causes allergic reactions
- Methemoglobinemia due to administration of large doses of prilocaine due to its metabolite O-toluidine, which oxidizes hemoglobin to methemoglobin.
- Dose dependant systemic toxicity:

Lignocaine plasma concentration (microgram/ml)	**systemic effect**
1-5	Analgesia
5-10	Circumoral numbness, skeletal muscle twitching, tinnitus, systemic hypotension, prolongation of P-R interval, myocardial depression
10-15	Seizures and unconsciousness
15-25	Apnea,coma
>25	Cardiovascular depression

- Circumoral numbness and tinnitus may be due to drug distribution to highly vascular tissues
- When plasma concentrations increase, it crosses the blood brain barrier and produce CNS toxicity
- Skeletal muscle twitching is the first evident in the face for imminence of tonic clonic seizures which is due to depression of inhibitory cortical pathways

CARDIOTOXICITY :

High plasma concentration of the drug blocks cardiac sodium channels

Less than 5mics/ml plasma concentration of lignocaine decreases the rate of spontaneous phase 4 depolarisation. 5 to 10 mics/ml produces arteriolar smooth muscle relaxation and direct cardiac depression

Bupivacaine will cause rapid profound cardiovascular depression and the dose required for irreversible cardiovascular collapseis lower for bupivacaine than lignocaine.

TREATMENT:

- Airway management
- Seizures can be controlled by benzodiazepines.if persists,small doses of succinylcholine or neuromuscular blockers given to minimize acidosis and hypoxemia.
- If Cardiac arrest occurs,initiate advanced cardiac life support

  Adrenaline 10-100microgram bolus can be considered

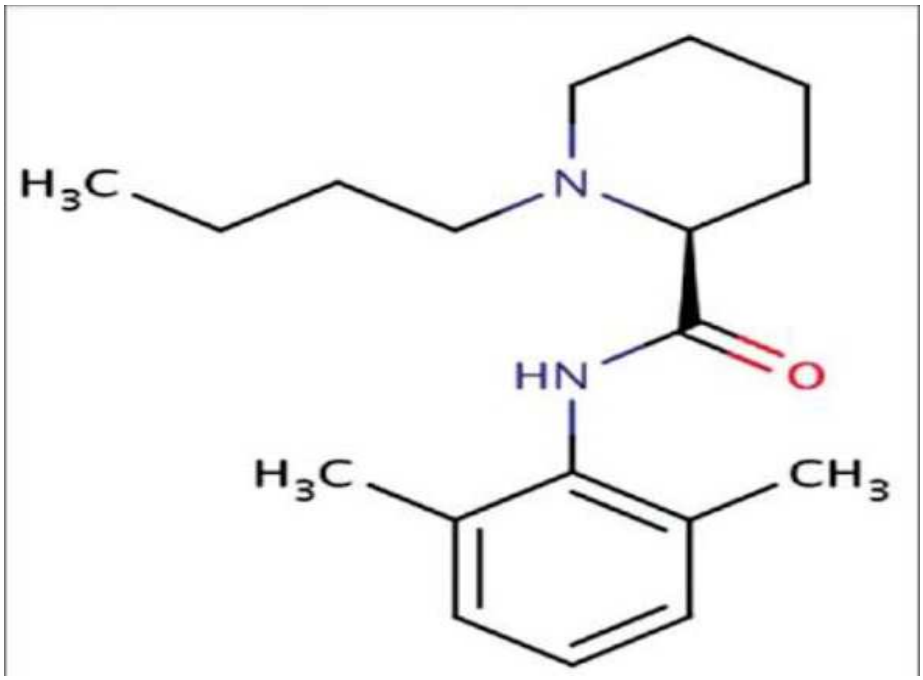
- Avoid calcium channel blockers,beta blockers and vasopressin not recommended
- LIPID EMULSION THERAPY:

Rapid bolus of Intra lipid 20%, 1.5 mL/kg (or approximately 100 mL for adults), administering without delay, start an infusion of 0.25 mL/kg/min for the next 10 minutes.

- Use of rapid-response extracorporeal membrane oxygenator or cardiopulmonary bypass may be advised.

LEVOBUPIVACAINE

It is an amide moderate duration acting local anaesthetic drug. It is the pure S-enantiomer of bupivacaine.



[2S] 1-butyl-N-2,6 dimethylphenyl piperidine -2-carboxamide

(C18H28N20)

Mechanism of action: reversible blockade of sodium channels

PHARMACOKINETICS:

- The dose and route of administration of determines plasma concentration of the drug.
- Absorption depends on the vascularity of the tissue

PLASMA PROTEIN BINDING: more than 97% at concentrations between 0.1 to 1microgram/ml

METABOLISM: CYP 3A4 isoform & CYP 1A2 isoform metabolises levobupivacaine as 3-hydroxy levobupivacaine(major metabolite) and desbutyl levobupivacaine

EXCRETION: In urine as glucuronic acid and sulphate ester conjugates

The dose of levobupivacaine is expressed as bases but racemic mixture of bupivacaine as hydrochloride salts. This gives rise to 13% more of active substances than bupivacaine

PREPARATION:

It is available in 10ml ampoule for intrathecal injection-5mg/ml of 0.5% levobupivacaine Hydrochloride.

USAGE:

1.SURGICAL ANAESTHESIA

Epidural,intrathecal ,peripheral nerve block and local infiltration

2.PAIN MANAGEMENT

Continuous epidural infusion, Labour analgesia

DOSAGE &ADMINISTRATION

EPIDURAL ANALGESIA

- The maximum recommended single dose is 150mg and 400mg over 24hrs
- For labour analgesia,the dose shouldn't exceed 12.5mg/ml
- Continuous infusion of 0.25% levobupivacaine 15mg/hr produces effective postoperative analgesia
- Onset of sensory block adequate for surgery occurs in 10-15 min with a time to regression in the range of 6-9hrs.

WOUND INFILTRATION

- Post incisional wound infiltration with 0.125% levobupivacaine provides more effective &longer duration of analgesia and early mobilization
- Addition of tramadol provides good postoperative analgesia

PERIPERAL NERVE BLOCK

The longer duration of sensory block than ropivacaine and less toxicity makes it a better choice for peripheral nerve blocks

INTRATHECAL ANAESTHESIA

0.5% levobupivacaine 3ml (15mg) itself will cause moderate to complete block

Though onset of motor block is delayed it is less dense compared to bupivacaine with similar duration

The regression of motor block occurs earlier than bupivacaine

ONSET TIME: 18 to 30 min

MAXIMUM CEPHALAD SPREAD: T7-T8

DURATION OF SENSORY BLOCKADE: 4to 6hrs

MINIMUM EFFECTIVE DOSE: 2.75mg to 3.16mg

CONTRAINDICATIONS:

- General contraindications related to regional anaesthesia
- Patients with hypersensitivity to levobupivacaine
- For I.V. regional anaesthesia(Bier's block)
- Paracervical block in obstetrics due to the incidence of fetal bradycardia
- Used in caution with patients receiving class 3 antiarrhythmic drugs since their toxic effects may be additive.

OPIOID ANALGESICS

OPOS-greek word means-juice. Opium derived from the juice of papaver somniferum

CLASSIFICATION OF OPIOIDS :

Natural alkaloids-Phenanthrenes (morphine and codeine)

Benzylisoquinolines (papaverine)

Semisynthetic –Heroin

Dihydromorphone,

Morphinone

Thebaine derivatives (e.g., etorphine, buprenorphine)

Synthetic- morphinan derivatives (levorphanol),

Diphenyl or methadone derivatives (methadone, *d*-propoxyphene),

Benzomorphans (phenazocine, pentazocine),

Phenylpiperidine derivatives :

meperidine, fentanyl, alfentanil,sufentanil, and remifentanil.

OPIOID RECEPTORS:

The Three types of opioid receptors are named

μ for the morphine type,

κ for the ketocyclazocine type,

δ receptor - for enkephalins

Additional receptors

σ for the SKF10047 (*N*-allylnormetazocine) type

ε receptor - the binding site for β-endorphin

PHARMACOLOGICAL ACTIONS OF OPIOIDS AND OPIOID RECEPTORS:

	ACTIONS OF		
	RECEPTOR	**AGONIST**	**ANTAGONIST**
Supraspinal	μ, δ, κ	Analgesic	No effect
Spinal	μ, δ ,κ	Analgesic	No effect
Respiratory function	M	Decrease	No effect
Feeding	μ, δ ,κ	Increase feeding	Decrease feeding
Gastrointestinal tract	μ,κ	Decrease transit	No effect
Psychotomimesis	K	Increases	No effect
Sedation	μ, κ	Increases	No effect
Diuresis	K	Increases	-
HORMONE SECRETION:			
Prolactin	M	Increases release	Decreases release
Growth hormone	μor/and δ	Increases release	Decreases release
NEUROTRANSMITTER RELEASE:			
Acetylcholine	M	Inhibit	-
Dopamine	Delta	Inhibit	-

CHARACTERISTICS OF OPIOID RECEPTORS:

	μ	δ	κ	Nociceptin
Tissue bioassay	Guinea pig ileum	Mouse vas deferens	Rabbit vas deferens	—
Endogenous ligand	β-Endorphin, endomorphin	Leu-enkephalin, met-enkephalin	Dynorphin	Nociceptin
Agonist	Morphine, fentanyl, DAMGO	DPDPE, deltorphin,	Buprenorphine, pentazocine, U50488H	—
Antagonist	Naloxone, naltrexone	Naloxone, naltrindole	Naloxone, NorBNI	—
Coupled G protein	$G_{i/o}$	$G_{i/o}$	$G_{i/o}$	$G_{i/o}$
Adenylate cyclase	Inhibition	Inhibition	Inhibition	Inhibition
Voltage-gated calcium channels	Inhibition	Inhibition	Inhibition	Inhibition
Inward rectifier potassium channels	Activation	Activation	Activation	Activation

DPDPE, [d-penicillamine2, d-penicillamine5]enkephalin; *DAMGO*, [d-Ala2, MePhe4, Gly-ol8]enkephaline; *NorBNI*, norbinaltorphimine.

MECHANISM OF OPIOID ANALGESIA

- Ability to directly inhibit the ascending transmission of noxious

information from the spinal cord dorsal horn and to activate pain control circuits that descend from midbrain, via the rostral ventromedial medulla (RVM),to the spinal cord dorsal horn

- Opioid binds to receptor

  ⬇

  Activation of Gi protein

  ⬇

  Inhibits voltage gated Ca+ channel

  ⬇

  Inhibits neuronal excitability

  ⬇

  Pain modulation in periaqueductal grey matter

  ⬇

Removal of γ-aminobutyric acidergic(GABAergic) inhibition of Rostral ventromedial medullar projecting neurons in the Periaqueductal grey matter and spinally projecting neurons in the Rostral ventromedial medulla

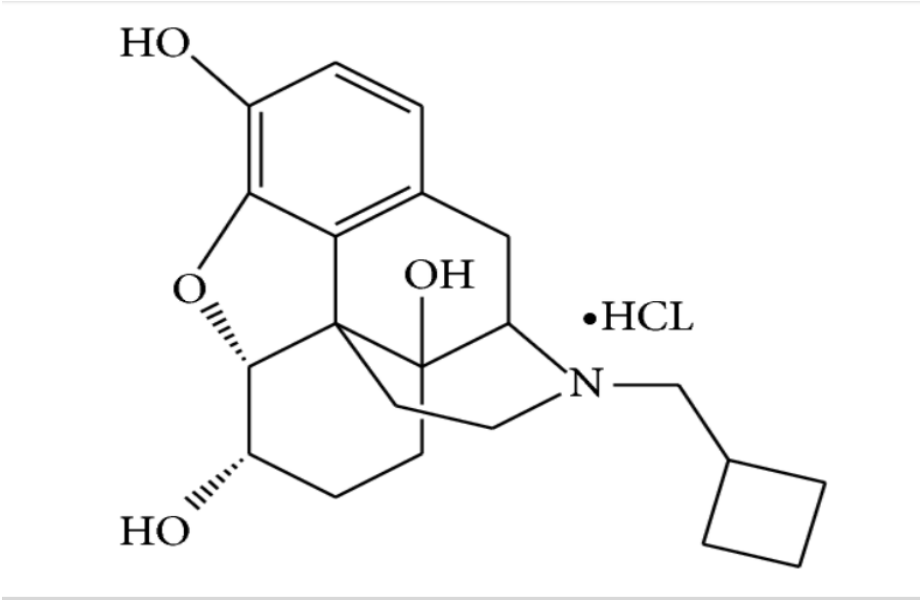
- In the spinal cord, opioids act at synapses either presynaptically or postsynaptically. Opioid receptors are mostly expressed in the substantia gelatinosa, where substance P release from the primary sensory neuron is inhibited by opioids.

- PERIPHERAL MECHANISM:

Immune cells infiltrating around the inflammation site release endogenous opioid-like substances, which act on the opioid receptors located on the primary sensory neuron.

NALBUPHINE

Nalbuphine is a semisynthetic opioid agonist antagonist. It is chemically related to oxymorphone and naloxone



(-)17-octobutylmethyl-4,5alpha epoxymorphinan-3,6 alpha,14-triol (C21H27NO4)

MECHANISM OF ACTION

Nalbuphine acts as an antagonist at the mu receptors and an agonist at the kappa receptors. Activation of supraspinal and spinal kappa receptors results in limited analgesia.

PHARMACOKINETICS

Nalbuphine is available only for parentral use.

METABOLISM in liver

ONSET –(rapid) 5 to 10 min

DURATION- (long) 3 to 6hrs

PLASMA ELIMINATION T1/2- 5hrs

POTENCY-equal as an analgesic to morphine &one fourth as potent as nalorphine as an antagonist

PREPARATION

It is available in 1ml ampoule has 10mg nalbuphine hydrochloride.

CEILING EFFECT-nalbuphine 10 mg dose produces analgesia similar to morphine more than 30 mg dose may produce respiratory depression, no further analgesic effect

SIDE EFFECTS

Most commonly-sedation

Dysphoria is less

Mild withdrawal symptoms

Limited ability to depress respiratory function

Naloxone – a specific antidote which may reverse the adverse effects &overdose effects

Nalbuphine doesn't increase systemic blood pressure,pulmonary artery pressure,heart rate and atrial filling pressures

USES:

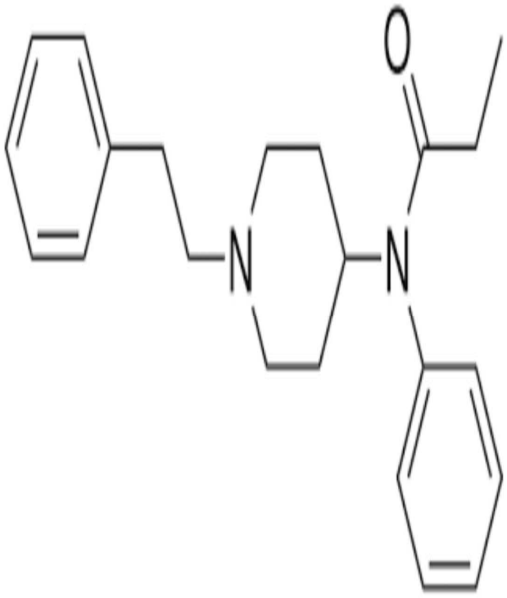
- Nalbuphine is an analgesic supplement for continuous sedation or balanced anaesthesia
- Used as an analgesic for postoperative and chronic pain
- Continuous infusion of 0.05-0.1mg/kg/min is useful to provide sedation and analgesia during myocardial revascularization
- It reverses the postoperative respiratory depression caused by fentanyl but maintains its analgesic effects. But evidence of recurrent hypoventilation occurs 2 to 3hrs later
- Potent antishivering effect so prevents /used for treatment of morphine induced pruritis
- Nalbuphine 4mg IV was as effective as ondansetran 8mg IV for prevention of intrathecal morphine induced nausea ,vomiting

LIMITATIONS

- It lacks the ability to attenuate cardiovascular and hormonal responses to tracheal intubation and surgical procedures

FENTANYL

It is a synthetic phenylpiperidine derivative tertiary amine opioid.Its analgesic effect is 75 to 125 times more potent than morphine.



MECHANISM OF ACTION:

Fentanyl is a highly selective mu opioid receptor agonist .It acts on presynaptic Gi protein coupled receptor and increases K+ conductance leads to hyperpolarization of cell membrane .This closes the voltage sensitive Calcium channels and decreases both pre and post synaptic responses

ROUTES AND DOSE OF ADMINISTRATION:

- Epidural route-50 to 100µ can be given. Spinal route-up to 25µ given because of its higher lipid solubility.

- For anaesthetic induction a loading dose of 2 to 6µ/kg can be given with other sedative hypnotics and maintanence of anaesthesia can be achieved by 0.5 to 5µ/kg/hr.
- For total intravenous analgesia the loading dose of fentanyl is 4 to 20µ/kg.maintenance infusion rate is 2 to10µ/kg/hr additional bolus-25 to 100µ can be given
- Produce surgical anesthesia fentanyl 50–150 µg/kg IV can be used
- Intramuscular 50 to 100µ for adults premedication dose.
- Transdermal therapeutic system delivers fentanyl at doses of 20,50,75,100µ/hr to achieve blood concentrations less than 1.0 to 2.0 ng/ml.peak concentration attained in 18hrs then becomes stable.
- To blunt the sympathetic response -1.5 to 3µ/kg IV 5min before surgical stimulation
- Oral transmucosal fentanyl citrate -5 to 20µ/kg. it consists of sweetened lozenge on a stick with fentanyl incorporated.it can be administered through transdermal iontophoretic delivery system.
- The plasma concentration required for postoperative analgesia is 1.5ng/ml

PHARMACOKINETICS:

Oral bioavailability is 33%.Transdermal delivary has 47% bioavailability in 24hrs and 94% in 48hrs.The lungs act as large inactive storage site for fentanyl with 75% of initial dose of the drug undergoes first pass pulmonary uptake.Its short duration of action reflects rapid redistribution

to skeletal muscles and fat so <80% of the drug leaves the plasma in lesser than 5min.

PLASMAPROTEIN BINDING: Fentanyl is 84-94% bound to plasma proteins

VOLUME OF DISTRIBUTION: larger volume of distribution-3to 5 lit/kg due to Greater lipid solubility and thus rapid passage to tissues than morphine

pKa of fentanyl is 8.4. At physiological pH 7.4 unionized is <10% and diffusion fraction is 1.5%.

METABOLISM: it is metabolized in the liver by N-demethylation and producing norfentanyl, hydroxypropionyl-fentanyl and hydroxypropionyl-norfentanyl. Metabolites are pharmacologicaly minimally active. CYP 450-CYP3A plays a major role in fentanyl metabolism.

EXCRETION: <10% of the drug excreted unchanged in the urine.

CLEARANCE -10-20 ml/kg/min. hepatic excretion ratio is 0.6-0.8.

ELIMINATION: t1/2α-1 to 2min. t1/2β-10to 20min.t1/2γ-2 to 4 hr.

CONTEXT SENSITIVE HALF TIME: After 4 hrs of infusion it is 260 min

Effect site (blood to brain) equilibration time-6.8 min. Fentanyl shows decrease in plasma concentration during cardiopulmonary bypass because the drug adheres to the bypass circuit thus elimination also prolonged.

PREPARATION:

It is prepared as 2ml ampoule -50µg fentanyl citrate.

CLINICAL USES:

- To provide intraoperative and postoperative Analgesia
- Neuroleptic analgesia can be given if it is combined with tranquilizer
- To provide patient controlled analgesia
- Premedication for anaesthesia
- Fentanyl is used in palliative care for pain relief
- Adjuvant in spinal and epidural anaesthesia
- Used for total intravenous anaesthesia
- To blunt the sympathetic response to laryngoscopic and surgical stimulation

CLINICAL EFFECTS:

CARDIOVASCULAR SYSTEM: Central vagal nucleus stimulation and decreasing sympathetic activity leads to Bradycardia and hypotension .It doesn't affect cardiac output,mean arterial pressure, pulmonary and systemic resistance. Depresses baroreceptor mediated reflex. Minimal histamine release than morphine

RESPIRATORY SYSTEM:

Directly depression brainstem respiratory center in a dose dependant manner and it decreases both tidal volume and respiratory rate(prolongs the expiratory time).

It decreases the change in PaCo2 sensitivity to respiratory centers and hypocapnic hyperventilation prolongs respiratory depression.

Potent antitussive property.

CENTRALNERVOUS SYSTEM:

Fentanyl can cause modest decrease in cerebral metabolic rate and intracranial pressure.It can produce analgesia without loss of consciousness. It releases cortical inhibition over the Edinger-Westphal nucleus, which leads to papillary constriction (miosis). Muscle rigidity (wooden chest phenomenon) occurs due to increase in muscle tone Which decreses chestwall compliance. Vocal cord closure is mainly responsible for the difficult bag and mask ventilation following administration of opioids. fentanyl decrease the minimal anaesthetic concentration required for volatile anaesthetic agents.

ENDOCRINE SYSTEM:

Opioids are reducing the stress response by modulating nociception at different levels of the neuronal pathway, and inhibits pituitary adrenal axis.

RENAL SYSTEM:

Antidiuresis and decreases electrolyte excretion due to μ receptor activation leads to urinary retention and it decreases the tone of detrusor muscle.

GASTROINTESTINAL SYSTEM:

Decreased gastric motility leads to decreased appetite and increased gastroesophageal reflux . Decreases pyloric tone leads to nausea and vomiting. Increased fluid absorption can cause hard, dry stools and constipation. It also

increases anal sphincter tone. As it increases Sphincter of Oddi tone,the biliary duct pressure increases and produce abdominal cramps.

SIDE EFFECTS:

Respiratory depression, nausea and vomiting, bradycardia, skeletal muscle rigidity and myoclonus ,seizure like activity without EEG changes, pruritis, urinary retention.

MATERIALS AND METHOD

MATERIALS AND METHODS

The study was submitted duly before the Institutional Ethical Committee and approval was obtained before starting the study.

STUDY DESIGN:

This is a Prospective Randomized double blinded study.

SAMPLE SIZE CALCULATION:

This study has included 60 female patients who were classified under American Society of Anaesthesiologists Physical Status 1 or 2 planned for elective lower abdominal gynaecological surgery

INCLUSION CRITERIA:

- 30 to 60 yrs of age adult female
- American Society of Anaesthesiologists Physical Status 1 or 2
- Elective lower abdominal gynecological surgery
- Patient who gave valid informed consent for the study

EXCLUSION CRITERIA:

- Patients posted for emergency surgery
- Patients with difficult airway
- Patients with Lack of written informed consent
- Coagulopathies and bleeding diathesis
- Impaired platelet function

- History of seizures and any neurological deficit
- Allergy to Local anaesthetic drugs
- Patient refusal.
- Patients with severe cardiovascular, respiratory, renal, hepatic diseases.
- Local infection at injection site

STUDY CENTER AND STUDY PERIOD:

Institute of Obstetrics and Gynaecology, Madras medical college,Chennai-600003. Duration of study is from September 2017-January 2018.

PREOPERATIVE ASSESSMENT:

All the 60 patients were examined duly on the day prior to surgery and preoperative assessment chart was checked. The Age, Height, Weight, Body mass index were measured & noted. The nutritional status and general condition of the patient and Airway examination and Spine examination were evaluated. Preoperative investigations were done: CBC, PT, PTT, INR, liver function tests, kidney function tests, fasting blood sugar, Electrocardiography and chest xray. Patients were explained about the Visual analog scale score which was used postoperatively for pain score assessment.

INFORMED WRITTEN CONSENT:

All 60 patients were informed about the nature of this study and its complications and valid informed written consent was obtained.

PREMEDICATION:

All the patients who were posted for elective lower abdominal gynecological procedure were fasted overnight and they were premedicated with Injection. Ranitine 50mg IM, Injection. Metaclopramide 10mg IM 45 mins before the surgery.

PREPARATION:

Patients were shifted inside the operation theatre and standard monitors like Non invasive blood pressure (NIBP),Electrocardiography(ECG),Pulse oximetry were connected and baseline values were recorded. A suitable Intravenous line was secured in patient's upper limb with 18G cannula and the patients were preloaded with 10ml/kg Crystalloid solution(Ringer lactate).Patients were randomly separated into either of two groups-Group A and Group B by Closed opaque envelop technique.

MATERIALS:

DRUGS

- Inj.Nalbuphine hydrochloride
- Inj.fentanyl
- Inj.0.5% levobupivacaine
- Normal saline
- Emergency drugs

EQUIPMENTS:

- 25G Quincke babcock needle
- Sterile drapes and sterile bowl
- Sterile gauze pieces
- Sponge holding forceps
- Sterile 2ml &5ml syringes

TECHNIQUE:

The patient was positioned in sitting position with leaning forward. Sterilisation of the local site was done. Using midline approach, Under strict aseptic precautions, subarachnoid block was given at L3-L4 intervertebral space with 25G quincke needle. After free flow of clear Cerebrospinal fluid the drug was injected at 0.2ml/sec.

GROUP A patients received 15mg (3ml) of 0.5% levobupivacaine and fentanyl 25µ-Total volume of drug is 3.5ml.

GROUP B patients received 15mg (3ml) of 0.5% levobupivacaine and nalbuphine 0-5mg-Total volume of the drug is 3.5ml

Patient immediately positioned to supine then Supplemental oxygen at 6 lit/min was administered through facemask. Patient's hemodynamcic parameters like non invasive blood pressure, heart rate, peripheral oxygen saturation were monitored and recorded during procedure and at regular intervals intraoperatively and postoperatively for 6hrs

POSITION FOR SPINAL BLOCKADE:

MONITORING:

- When Hypotension(systolic blood pressure less than 90mmHg or less than 20% from baseline) produced, it was managed with Crystalloids administration and Injection. Ephedrine 6mg IV bolus
- When Bradycardia (Heart rate less than 50 beats/min) occurred, it was managed with Injection. Atropine 0.6mg IV bolus
- Shievering was managed with warm IV fluids administration, warm blankets , Injection. Tramadol 50 mg slow IV
- Nausea managed with correction of hypotension and administration of Injection. Ondansetran 8mg IV bolus

ASSESSMENT OF BLOCKADE

SENSORY BLOCK**:**

It was assessed by pinprick method in the midclavicular line using 27G needle, every minute until the block reached T6 dermatomal level. After that level, level was checked every 2mins until maximum sensory block achieved

ONSET OF SENSORY BLOCKADE:

The time interval between the end of anaesthetic injection to loss of sensation to pinprick at T10 was noted

MOTOR BLOCK: It was assessed by modified Bromage scale

Onset of complete motor blockade was the time interval between the end of anaesthetic drug injection to grade 3 bromage scale reached, which was noted.

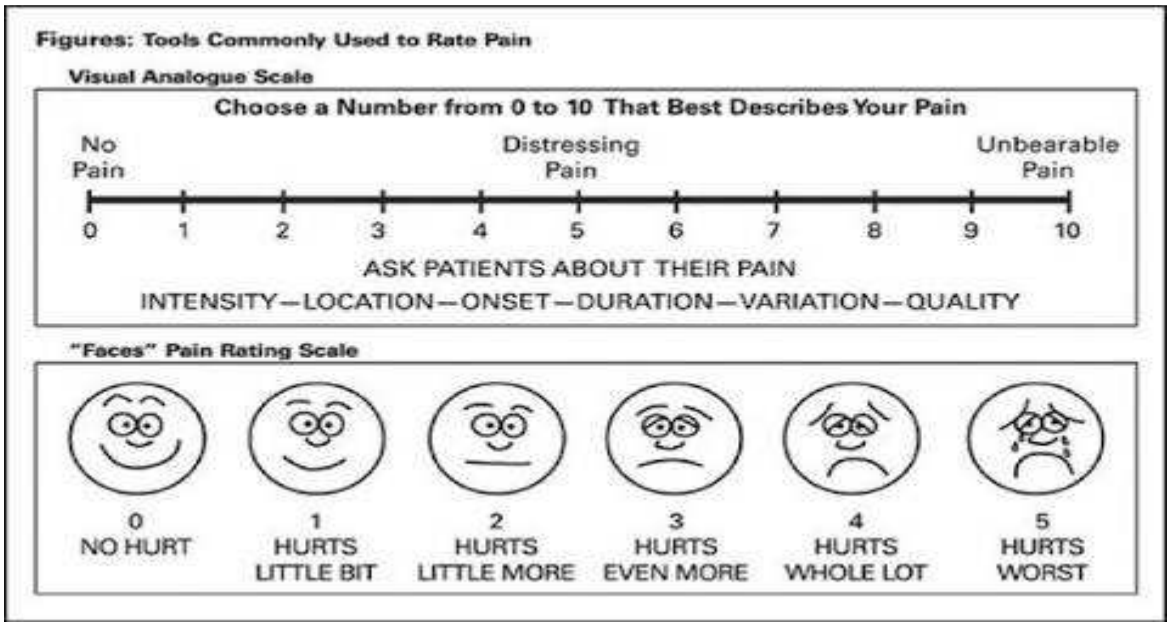
The duration of analgesia –the time from intrathecal injection to VAS greater than or equal to 1.

Surgery was proceeded when the sensory block reaches above T5.After completion of surgery ,both the motor and sensory blocks were assessed and Two segment regression time from the maximal complete anaesthesia to regression upto L1 was noted. Postoperatively the patient was followed up in the recovery and postoperative ward for hemodynamic parameters like respiratory rate, heart rate, noninvasive blood pressure, peripheral oxygen

saturation with pulse oximetry and patients pain score was assessed with Visual analog scale score.

VISUAL ANALOG SCALE:

It is one of a method of postoperative pain assessment



It was evaluated postoperatively and if VAS more than or equal to 4, Rescue analgesics were given Injection. Paracetamol/ Injection. Tramadol IV. The effective analgesic time is the time starting from intrathecal injection to VAS more than or equal to 4.Any complications were recorded and managed accordingly.

FLOW CHART

PREOPERATIVE ASSESSMENT OF THE PATIENT

↓

30-60yrs female under ASA PS 1&2 posted for elective lower abdominal surgery

↓

Valid informed consent obtained

↓

Patient shifted to operation theatre

↓

WHO checklist followed

↓

Groups choosen by closed envelope method

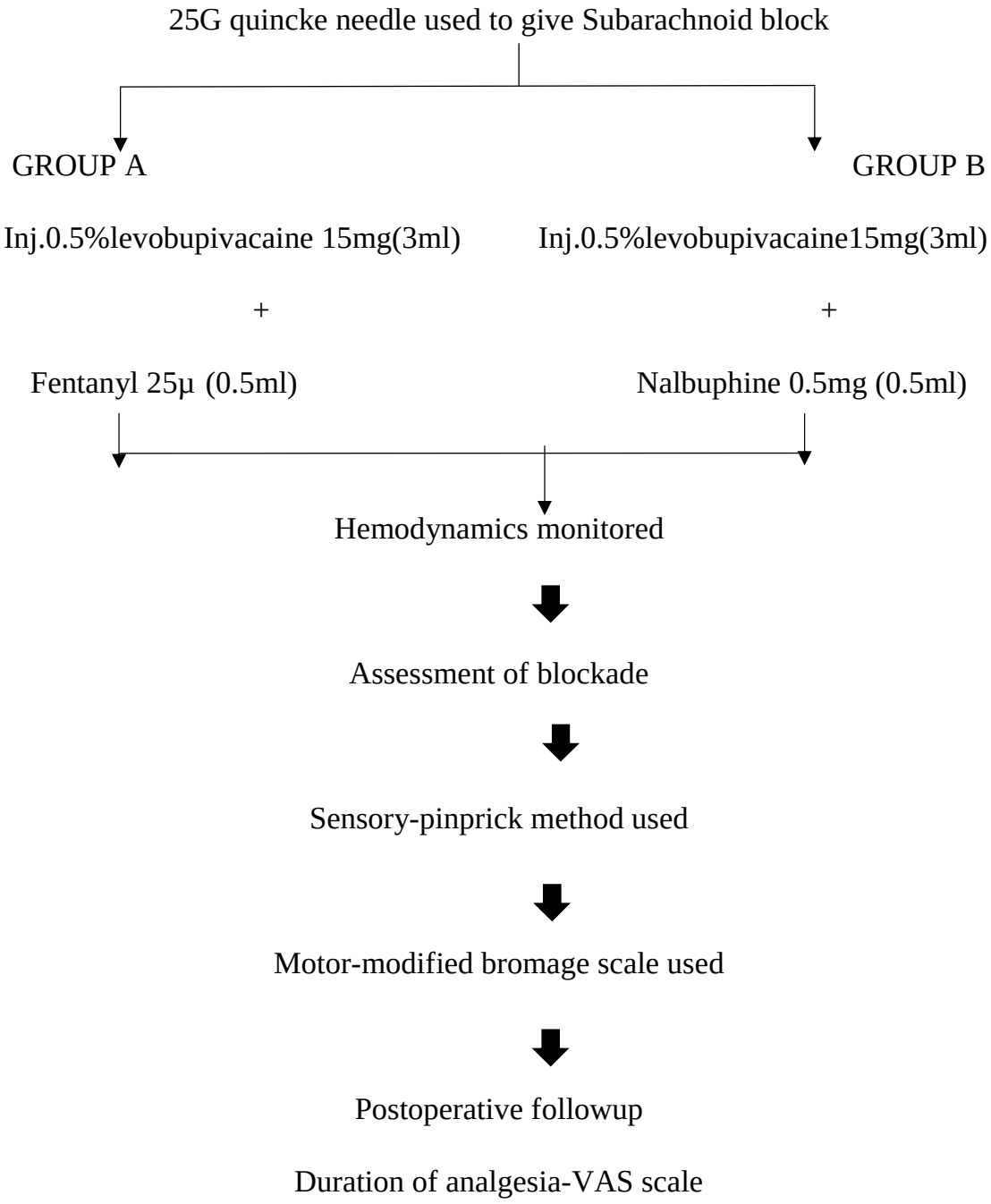
↓

ECG,NIBP and pulse oximetry connected to the patient

↓

18G IV access done and preloading with RL 100ml/kg given

↓


25G quincke needle used to give Subarachnoid block
GROUP A
GROUP B
Inj.0.5%levobupivacaine 15mg(3ml)
+
Fentanyl 25µ (0.5ml)
Inj.0.5%levobupivacaine15mg(3ml)
+
Nalbuphine 0.5mg (0.5ml)
Hemodynamics monitored
Assessment of blockade
Sensory-pinprick method used
Motor-modified bromage scale used
Postoperative followup
Duration of analgesia-VAS scale

OBSERVATION AND

RESULTS

OBSERVATION AND RESULTS

Sample size was calculated by n.master 2.0 software. Sample size was based on clinical trials, hypothesis equivalence/bioequivalence-parallel design. Equivalence margin-1,observed/expected difference-0.68,standard deviation is 0.5,effect size-0.64,Power(1-β)-80,α-error(%)-5,Group A-30,Group B-30.For statistical analysis Calculations were done using PS Power and Sample Size Calculations Software, version 3.0.11 for MS Windows. The demographic data of the patients were studied in both groups and the analysis revealed no significant difference observed between the two groups.

Results were expressed as means ± standard deviation of the means (SD) or number (%). Comparison of different parameters in the both groups was performed using unpaired t test. Comparison of the categorical data was done using Chi square test. The data were considered significant if p value - equal to or less than 0.05 and highly significant if p value is <0.01.” Statistical analysis was done with the help of the SPSS computer program -version 12 windows”.

GROUP A-FENTANYL+ LEVOBUPIVACAINE

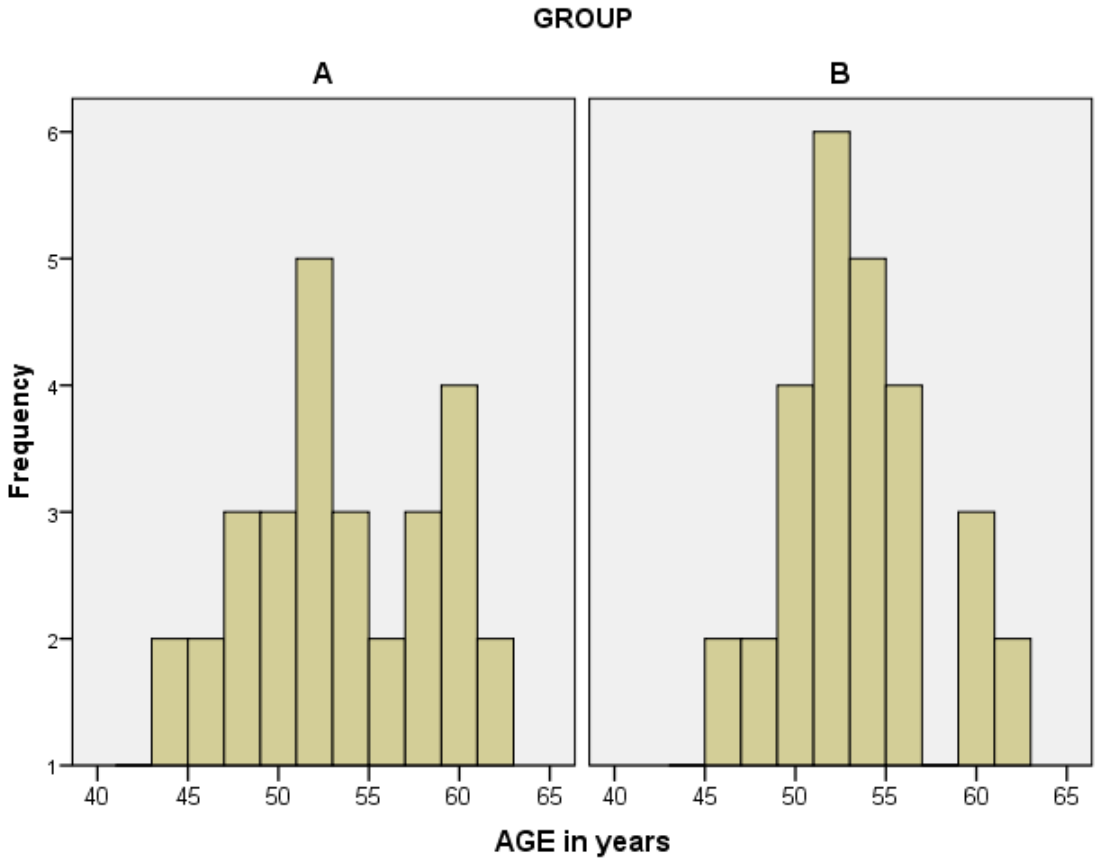
GROUP B-NALBUPHINE+LEVOBUPIVACAINE

Table 1:-MEAN AGE- in years

	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
AGE	A	30	52.43	5.50	0.764
	B	30	52.83	4.72	

The mean age distribution is similar in both the groups and the p value is 0.764 which is more than 0.5.It is not significant.

AGE DISTRIBUTION



This study was conducted among female patients only .So there is no comparison in sex between two groups.

Table 2:- WEIGHT AND HEIGHT DISTRIBUTION

	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
WT	A	30	56.20	3.87	0.076
	B	30	57.90	3.41	
HT	A	30	161.83	5.78	0.913
	B	30	161.67	6.01	

The mean weight and height distribution between the two groups are identical and p value for weight distribution is 0.076 and height distribution is 0.053 Hence the p value is more than 0.5 and no significance in weight and height distribution among both the groups.

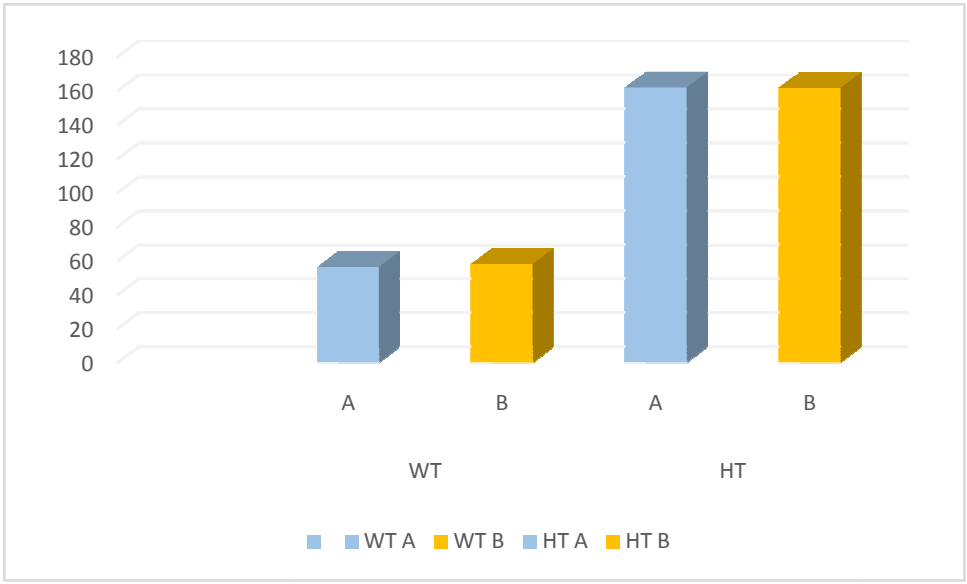


Table 3:- ASA PS DISTRIBUTION

GROUP	ASAPS		Total	Fisher exact p value
	1	2		
A	26(86.66%)	4 (13.33%)	30 (100%)	0.238
B	28 (93.30%)	2 (6.67%)	30 (100%)	
Total	54 (90%)	6 (10%)	60 (100%)	

ASA PS-American Society of Anaestheiologist Physical Status Classification

The ASA PS between the two groups were similar with p value 0.238 which is more than 0.05.This shows no significance between the groups.

Table 4:- DURATION OF SURGERY

	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
Duration of Surgery (min)	A	30	102.07	7.31	0.899
	B	30	100.07	7.01	

The duration of surgery is 102.07 ±7.31 in group A and 100.07 ±7.01 in group B. They are similar in both the groups with p value 0.899 .It is more than more than 0.05.So no significance between the groups in duration of surgery.

Table 5:-ONSET OF SENSORY BLOCKADE

ONSET OF SENSORY BLOCK		GROUP				p value by Chi sq test
		A		B		
		Count	%	Count	%	
30 sec	**0**	30	100.0%	30	100.0%	1
1 min	**T11**	7	23.3%	6	20.0%	0.754
	T12	23	76.7%	24	80.0%	
2 min	**T10**	27	90.0%	27	90.0%	0.665
	T11	3	10.0%	3	10.0%	
3 min	**T10**	26	86.7%	26	86.7%	0.647
	T8	4	13.3%	4	13.3%	
4 min	**T10**	0	0.0%	2	6.7%	0.081
	T6	3	10.0%	0	0.0%	
	T8	27	90.0%	28	93.3%	
5 min	**T5**	4	13.3%	0	0.0%	0.645
	T6	26	86.7%	23	76.7%	
	T8	0	0.0%	7	23.3%	
6 min	**T5**	26	86.7%	24	80.0%	0.488
	T6	4	13.3%	6	20.0%	
7 min	**T5**	30	100.0%	30	100.0%	1

At 2 mins ,the onset of sensory blockade to the T10 level achieved with p value 0.665 which shows no significance. The onset of sensory blockade to T6 achieved by 26 patients in 5 mins in group and 23 persons in 5 mins in group B with p value 0.645.it is more than 0.05.So it is statisticaly not significant.

Table 6:- ONSET OF MOTOR BLOCKADE:-

ONSET OF MOTOR BLOCK		GROUP				p value by Chi sq test
		A		B		
		Count	%	Count	%	
30 sec	**0**	30	100.0%	30	100.0%	1
1 min	**L1**	30	100.0%	30	100.0%	1
2 min	**L1**	4	13.3%	3	10.0%	0.784
	T12	26	86.7%	27	90.0%	
3 min	**T10**	3	10.0%	4	13.3%	0.887
	T12	27	90.0%	26	86.7%	
4 min	**T10**	27	90.0%	28	93.3%	0.081
	T12	0	0.0%	2	6.7%	
	T8	3	10.0%	0	0.0%	
5 min	**T10**	4	13.3%	0	0.0%	0.057
	T7	0	0.0%	28	93.3%	
	T8	26	86.7%	2	6.7%	
6 min	**T7**	24	80.0%	28	93.3%	0.665
	T8	6	20.0%	2	6.7%	
7 min	**T7**	30	100.0%	30	100.0%	1

The onset of motor blockade to L1 is achieved by 4 persons(13.3%) in group A and 3 persons (10.0%) in group B at 2mins,The onset of complete motor at 5mins is achieved by 26 patients in fentanyl group (86.7%) and 15 patients in nalbuphine group (50.0%) with p value 0.057.So there is no stastistical significance in onset of complete motor block in both the groups.

Table 7:- 2 SEGMENT REGRESSION TIME OF SENSORY BLOCK AND DURATION OF MOTOR BLOCKADE DISTRIBUTION:

	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
2SRT OF SB min	A	30	122.47	1.74	0.637
	B	30	123.53	1.79	
DMB min	A	30	126.87	2.92	0.890
	B	30	126.53	2.92	

The two segment regression time is earlier in group A but it is statistically not significant. It has p value 0.637 which is more than 0.05.The duration of motor blockade also shows no significance between the two groups with p value 0.890 -it is more than 0.05.

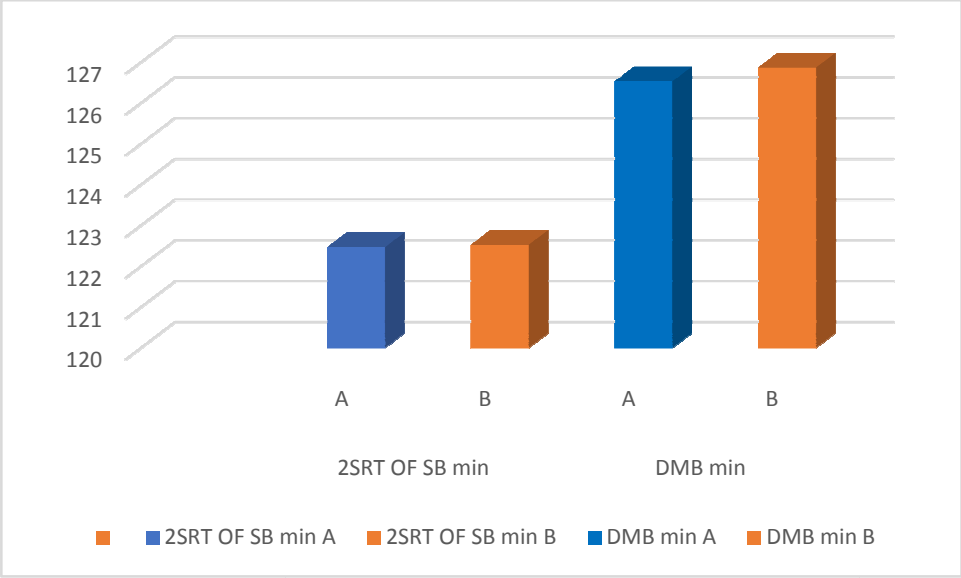


Table 8:-PERIOPERATIVE SYSTOLIC BLOOD PRESSURE DISTRIBUTION

PERI OPERATIVE SBP	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
BL	A	30	115.60	3.61	0.940
	B	30	113.60	3.49	
DP	A	30	110.53	4.74	0.750
	B	30	104.53	4.04	
INCISION	A	30	97.93	1.78	0.097
	B	30	98.57	1.01	
ES	A	30	118.90	10.99	0.584
	B	30	120.40	10.08	
0 hr	A	30	116.87	16.75	0.567
	B	30	119.23	15.02	
1 hr	A	30	121.60	10.27	0.790
	B	30	123.97	10.25	
2 hrs	A	30	120.63	5.13	0.056
	B	30	122.77	2.82	
3 hrs	A	30	120.80	6.30	0.055
	B	30	123.37	2.94	
4 hrs	A	30	120.63	5.13	0.112
	B	30	122.43	3.31	
6 hrs	A	30	114.13	3.84	0.735
	B	30	113.80	3.75	

The group A patients developed decrease in systolic blood pressure more than group B.But p value is more than 0.05.So there is no statistical significance in perioperative systolic blood pressure changes between the two groups. Fentanyl produced decreased systolic blood pressure than nalbuphine with no statistical significance.

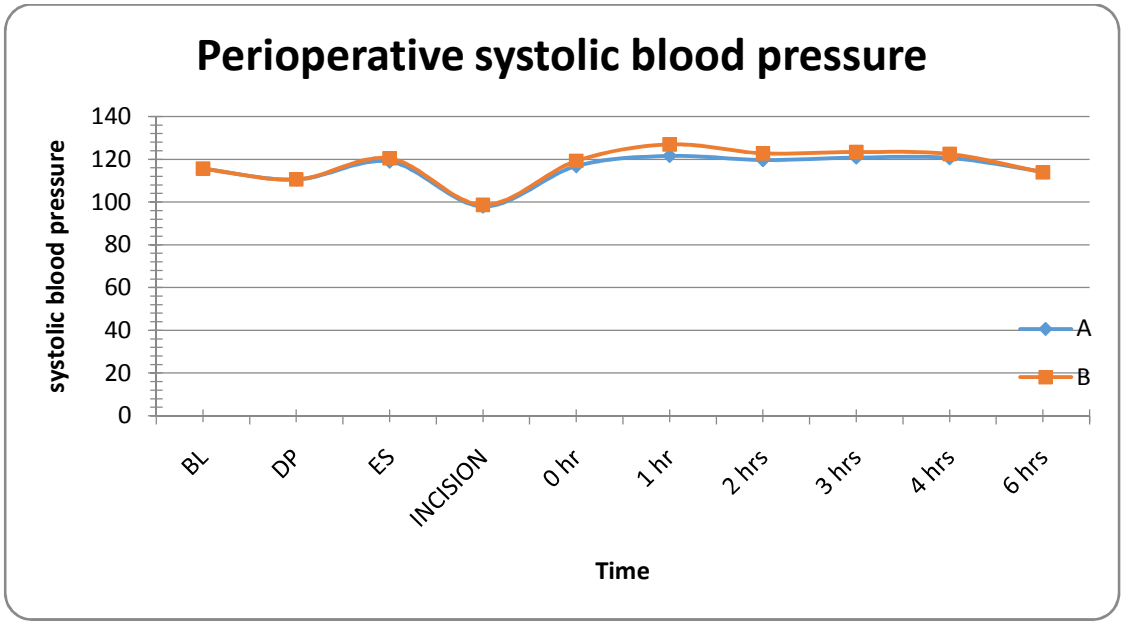


Table 9 :-PERIOPERATIVE DIASTOLIC BLOOD PRESSURE

PERI OPERATIVE DBP	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
BL	A	30	71.97	3.93	0.527
	B	30	70.97	3.05	
DP	A	30	72.70	3.10	0.862
	B	30	72.83	2.83	
INCISION	A	30	59.33	1.60	0.327
	B	30	59.73	1.53	
ES	A	30	68.67	4.59	0.322
	B	30	69.67	3.00	
0 hr	A	30	69.03	5.98	0.521
	B	30	70.00	5.60	
1 hr	A	30	76.83	6.33	0.061
	B	30	77.50	2.41	
2 hrs	A	30	78.10	6.08	0.077
	B	30	74.00	2.54	
3 hrs	A	30	78.87	5.75	0.056
	B	30	81.27	2.82	
4 hrs	A	30	81.07	6.05	0.056
	B	30	80.97	3.47	
6 hrs	A	30	81.50	6.52	0.060
	B	30	84.43	2.87	

The perioperative diastolic blood pressure changes are not statistically significant between both group A and B. It has p value more than 0.05.Fentanyl group produces decreased diastolic blood pressure at 0hr and 1 hr in postoperative period but it has no significance over nalbuphine group.

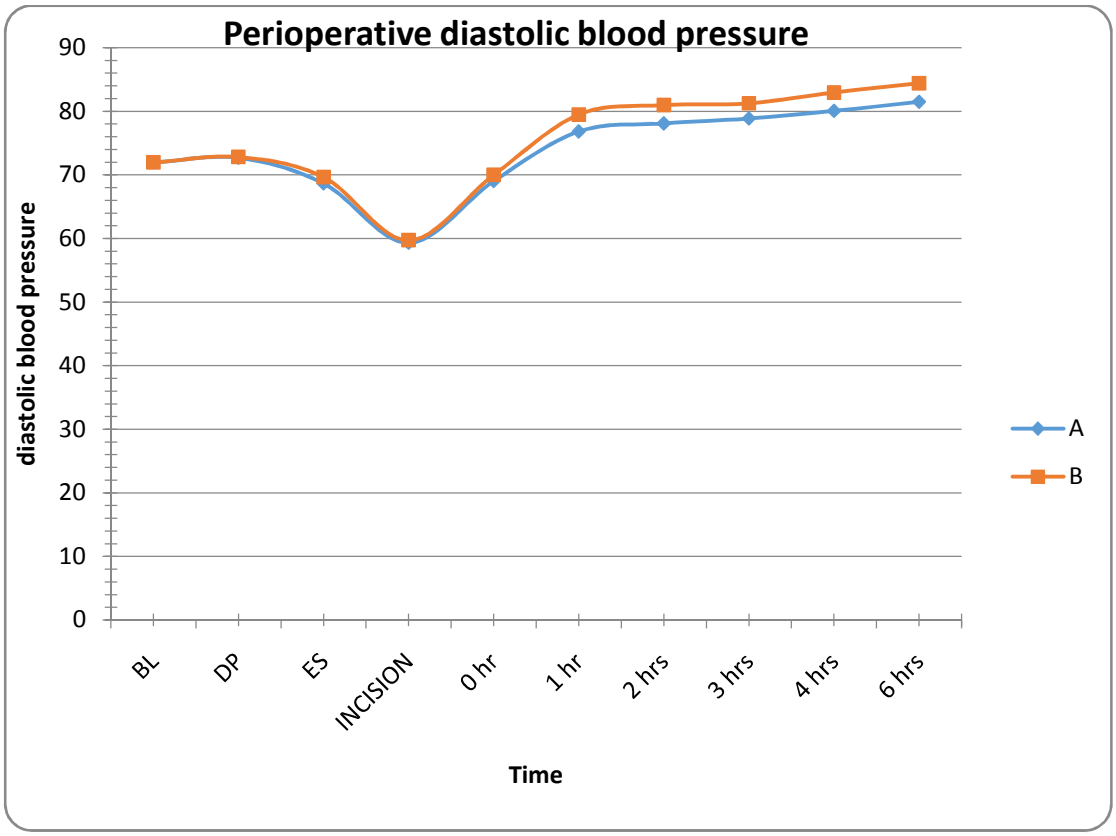


Table 10:-PERIOPERATIVE MEAN ARTERIAL PRESSURE

PERI OPERATIVE MAP	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
BL	A	30	86.54	2.87	0.880
	B	30	86.66	3.05	
DP	A	30	85.13	2.75	0.601
	B	30	85.49	2.49	
INCISION	A	30	72.62	2.27	0.867
	B	30	72.70	1.06	
ES	A	30	85.33	6.30	0.407
	B	30	86.57	5.15	
0 hr	A	30	85.03	9.37	0.708
	B	30	85.94	9.38	
1 hr	A	30	91.41	7.62	0.068
	B	30	92.39	3.28	
2 hrs	A	30	91.83	5.95	0.060
	B	30	93.90	3.63	
3 hrs	A	30	92.78	5.62	0.650
	B	30	93.28	4.50	
4 hrs	A	30	93.52	5.21	0.069
	B	30	94.98	2.67	
6 hrs	A	30	92.55	4.60	0.083
	B	30	94.20	2.20	

MAP- Mean Arterial Pressure.

The Mean Arterial Pressure changes between both the groups has no statistical significance with p values are more than 0.05 .Fentanyl produces decrease in Mean Arterial Pressure than nalbuphine produces with no statistical significance.

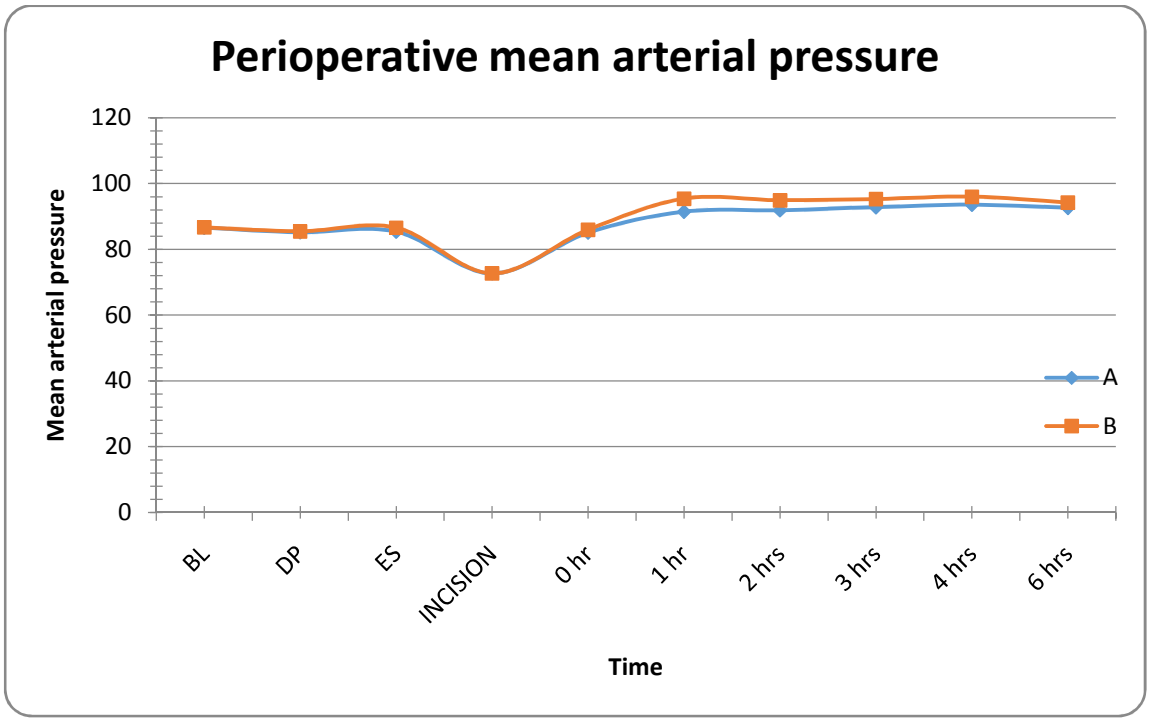


Table 12:-PERIOPERATIVE HEART RATE

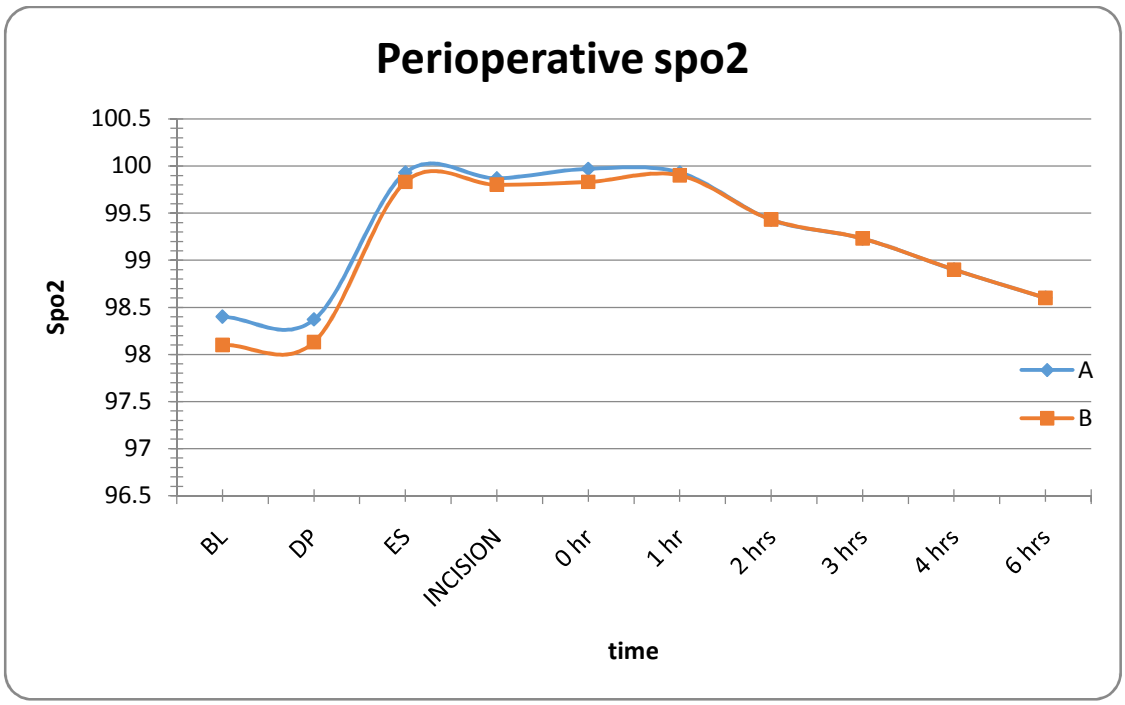
PERI OPERATIVE HEART RATE	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
BL	A	30	86.13	2.97	0.867
	B	30	85.33	5.77	
DP	A	30	86.13	2.01	0.657
	B	30	87.13	2.61	
INCISION	A	30	80.66	3.24	0.337
	B	30	81.20	4.24	
ES	A	30	80.10	3.58	0.297
	B	30	79.30	1.78	
0 hr	A	30	80.80	2.78	0.095
	B	30	81.30	3.78	
1 hr	A	30	90.30	1.51	0.767
	B	30	91.33	2.53	
2 hrs	A	30	91.43	1.55	0.887
	B	30	89.86	3.54	
3 hrs	A	30	90.56	1.57	0.055
	B	30	91.87	1.69	
4 hrs	A	30	85.10	2.96	0.776
	B	30	86.14	3.96	
6 hrs	A	30	81.03	2.89	0.532
	B	30	80.43	2.09	

The fentanyl and nalbuphine groups produce similar changes in heart rate which is statistically not significant due to p value more than 0.05.

Table 13:-PERIOPERATIVE SPO2 CHANGES:

PERI OPERATIVE SpO2	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
BL	A	30	98.40	0.56	0.052
	B	30	98.10	0.61	
DP	A	30	98.37	0.49	0.095
	B	30	98.13	0.57	
INCISION	A	30	99.87	0.43	0.577
	B	30	99.80	0.48	
ES	A	30	99.93	0.25	0.235
	B	30	99.83	0.38	
0 hr	A	30	99.97	0.18	0.090
	B	30	99.83	0.38	
1 hr	A	30	99.93	0.25	0.647
	B	30	99.90	0.31	
2 hrs	A	30	99.43	0.78	0.740
	B	30	99.30	0.68	
3 hrs	A	30	99.33	0.73	0.747
	B	30	99.23	0.68	
4 hrs	A	30	98.90	0.31	0.647
	B	30	99.30	0.28	
6 hrs	A	30	98.90	0.58	0.890
	B	30	98.79	0.66	

The perioperative arterial saturation has not produced significant changes between the group A and B. They have p value more than 0.05 and not statistically significant.



Fentanyl and nalbuphine both has no effect on the peripheral arterial oxygen saturation.

Table 14:-PERIOPERATIVE RESPIRATORY RATE

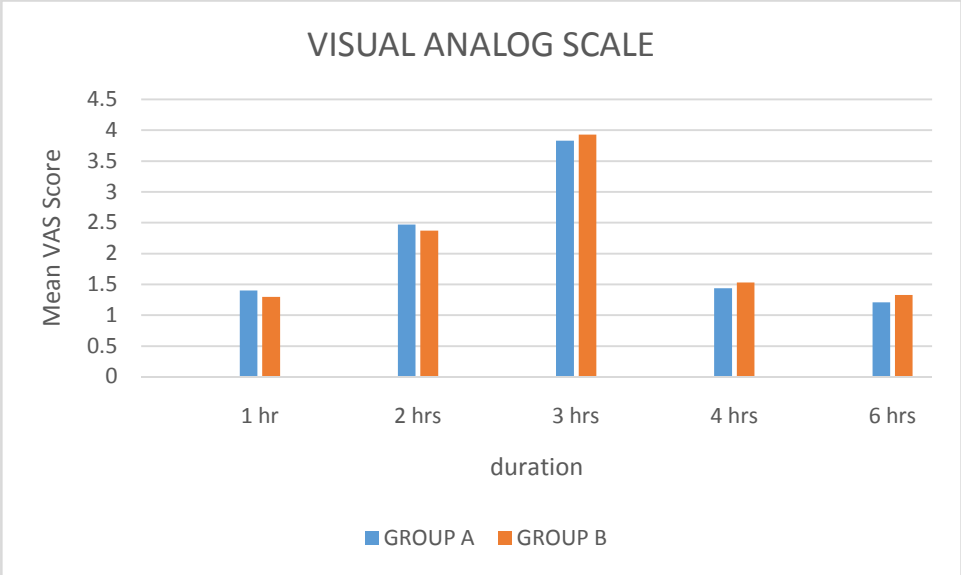
POST OP RR	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
0 hr	A	30	12.80	0.89	0.770
	B	30	12.73	0.87	
1 hr	A	30	12.80	0.89	0.772
	B	30	12.67	0.88	
2 hrs	A	30	12.73	0.91	0.774
	B	30	12.67	0.88	
3 hrs	A	30	12.73	0.91	0.673
	B	30	12.80	0.89	
4 hrs	A	30	12.73	0.91	0.774
	B	30	12.67	0.88	
6 hrs	A	30	12.63	0.57	0.574
	B	30	12.87	0.68	

Both fentanyl and nalbuphine groups had no change in respiratory rate during perioperative period with statistical significance. It has p value more than 0.05.

Table 15:- VISUAL ANALOG SCALE SCORE

	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
1 hr	A	30	1.40	0.50	0.425
	B	30	1.30	0.47	
2 hrs	A	30	2.47	0.57	0.470
	B	30	2.37	0.49	
3 hrs	A	30	3.83	0.38	0.565
	B	30	3.93	0.48	
4 hrs	A	30	1.43	0.49	0.545
	B	30	1.33	0.69	
6 hrs	A	30	1.21	0.51	0.445
	B	30	1.53	0.41	

The mean VAS score is around 4, at 3 hours in the post operative period, in both Fentanyl and Nalbuphine groups . There is no statistical significance between Fentanyl and Nalbuphine groups in visual analog scale score since they have p values more than 0.05.Rescue analgesia in the form of Injection. Paracetamol /Injection. Tramadol IV is given to the patients when VAS score is more than or equal to 4.



It shows that postoperative analgesia is similar in both fentanyl and nalbuphine groups.

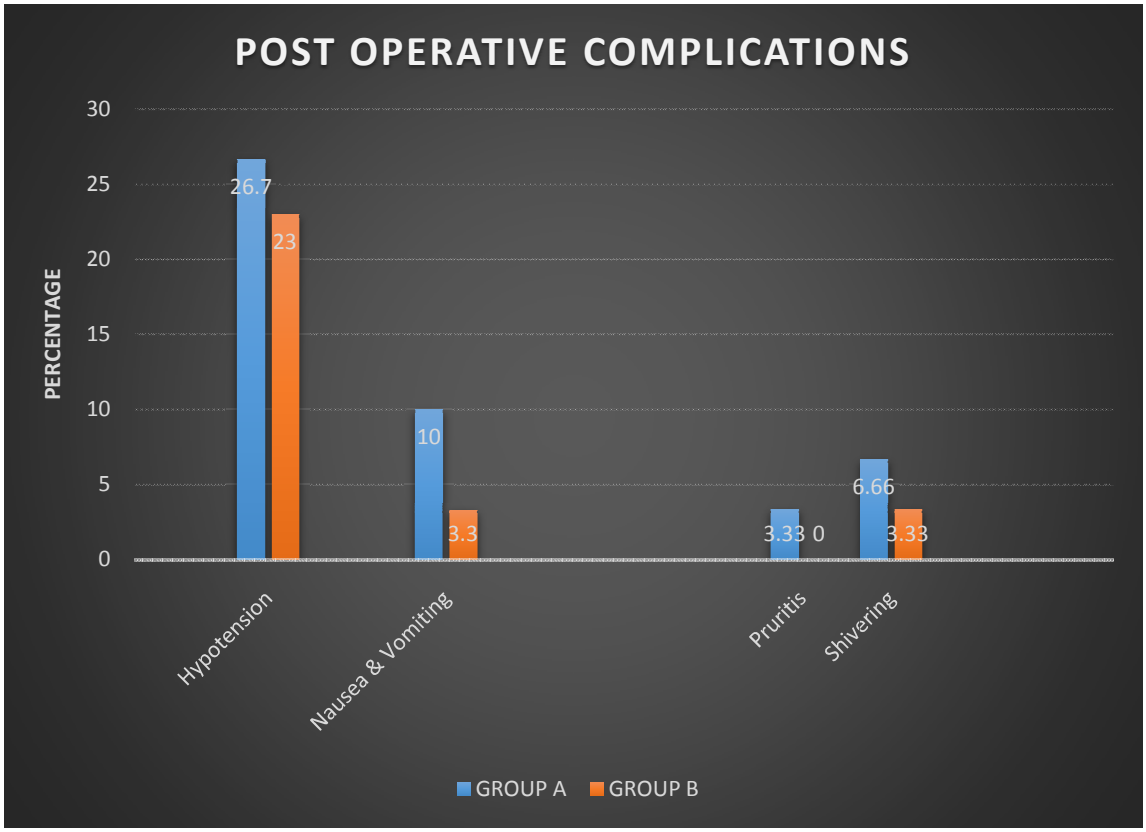
Table 16:-POST OPERATIVE COMPLICATIONS

POST OP COMPLICATIONS AT 0 HR	GROUP		P-value
	A	B	
Hypotension	8 (26.70%)	6 (23%)	0.542
Nausea & Vomiting	3 (10%)	1 (3.3%)	0.301
Pruritis	1 (3.33%)	0 (0%)	0.313
Shivering	2 (6.66%)	1 (3.33%)	0.554

In Fentanyl group , 8 persons had hypotension and in nalbuphine group 6 persons had hypotension and its p value is 0.542 which is statistically not significant. The hypotension was managed with crystalloids and Inj. Ephedrine 6 mg IV dose in fentanyl group 3(10%) patients had nausea and vomiting as side effect but in nalbuphine group only one patient has this side effect .It has no statistical significance with p value 0.313.The nausea and vomiting was managed with crystallois and Inj.ondansetran 8mg IV

In fentanyl group one patient had mild pruritis but in nalbuphine group,no pruritis developed.But it was not statistically significant.

In shivering was more in fentanyl (6.66%) than nalbuphine group (3.33%) but its not statistically significant.

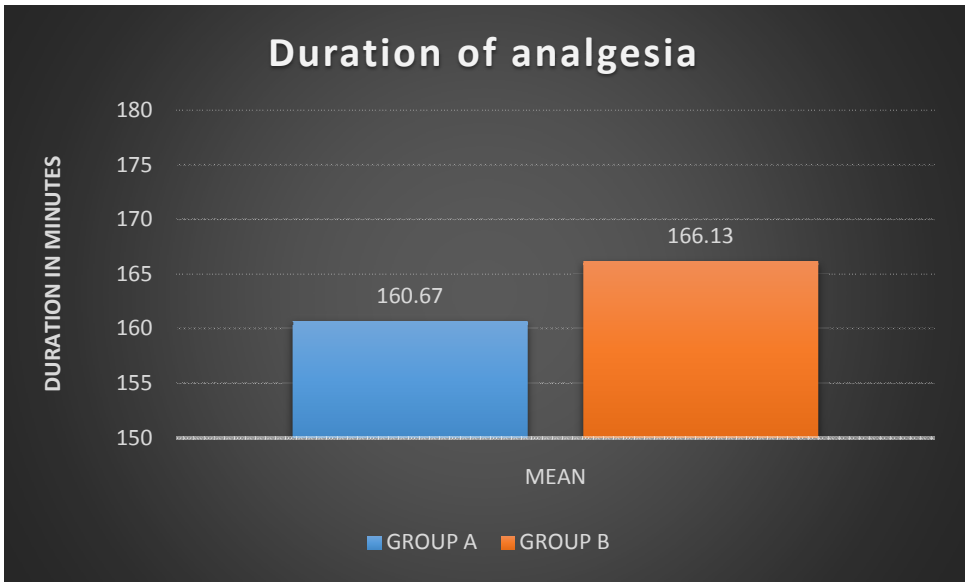


It shows both fentanyl and nalbuphine has no statistical significance in side effects

Table 17:- DURATION OF ANALGESIA

	GROUP	N	MEAN	STD. DEVIATION	p VALUE BY 't' TEST
Duration of Analgesia (min)	A	30	160.67	4.85	0.059
	B	30	166.13	6.52	

The power analysis was based on the difference in duration of analgesia between both the groups. The duration of analgesia is prolonged in nalbuphine group (166.13±6.52) than fentanyl group (160.67± 4.85) with p value 0.059 which is not statistically significant.



There is no statistical significance in duration of analgesia between nalbuphine and fentanyl.

DISCUSSION

DISCUSSION

Regional anaesthesia is most widely technique for infra umbilical surgeries .It is preferred over general anaesthesia because general anaesthesia is associated with increased mortality rate.

Incidence of high regional block and local anaesthetic toxicity are the causes of mortality with regional technique. Reduction in the doses of local anesthetic dose, the use of new techniques to avoid higher blocks and better local anesthetic toxicity management are the desired goals for decreasing mortality associated with regional anesthesia.

Varying techniques and drug regimens were used over years to improve the quality of spinal anaesthesia. Opioid adjuvants acts as synergistic to local anaesthetics and prolongs the duration of anaesthetic effect by increasing intensity of sensory block. These adjuvants acts on dorsal horn level in spinal cord and causes segmental blockade.

These opioid adjuvants allows early ambulance of the patient and prolonged postoperative analgesia due to their sympathetic and motor sparing effect. They also reduce the dose of local anaesthetics and decrease local anaesthetic toxicity.

Respiratory depression is the most dangerous side effect of opioids with pruritis being commonest. Other side effects are nausea and vomiting, hypotension and shivering.

Levobupivacaine was used as a local anaesthetic because it produces faster onset of anaesthesia .It causes less density in motor blockade than bupivacaine and also lesser side effects like cardiotoxicity.

Fentanyl –a pure mu opioid receptor. It produces better analgesia in smaller doses compared to other opioid drugs .Also it causes better hemodynamic profile. Pruritis is common with fentanyl .

Nalbuphine is a mixed kappa agonist and mu opioid receptor antagonist. It causes better analgesia with lesser respiratory depression.

Gangandeep singh et al conducted a study among 80 pregnant women posted for elective cesarean section who were divided into group A for them intrathecal 0.5%levobupivacaine with fentanyl 25microgram given and group B for them intrathecal 0.5% levobupivacaine given. They evaluvated the mean onset time of sensory blockade for group A is 2.5±0.2min but for group B - 5.82±2.7min ,Mean time to achieve complete sensory blockade for group A-6.8±2.3min and for group B-9.2±1.8min. Mean two segment regression time for group A-96.61min and group B-92.7±18.5min.they observed that the combination of fentanyl with levobupivacaine has achieved earlier complete sensory and motor blockade than levobupivacaine alone group. Also levobupivacaine with fentanyl reduced the need of postoperative analgesics.

Regarding the dose of nalbuphine, In 2011,Mukherjee et al conducted a study on 100 patients undergoing elective lower limb orthopaedic surgery under subarachnoid block. They used different doses of intrathecal nalbuphine

(200,400,800 micrograms) with 0.5% hyperbaric bupivacaine for Group A,B, and C respectively. They concluded that the duration of sensory block and effective analgesia were prolonged with doses of 400microgram (group B) and 800micrograms (group C) of nalbuphine with bupivacaine but higher doses of nalbuphine produced higher side effects. Hence we used 0.5mg nalbuphine intrathecal dose.

Suman chatterjee et al conducted a study among 96 patients undergone infra umbilical surgeries. They divided them into 3 groups. Group L received intrathecal 0.5% isobaric levobupivacaine 2.8ml +0.4ml normal saline, Group LB received intrathecal 0.5%levobupivacaine 2.8 ml + butorphanol 25microgram,Group LN received 0.5% levobupivacaine 2.8 ml + nalbuphine 0.4mg.The onset of sensory block was same in LB and LN group than group L but motor blockade was faster in Group LN .effective analgesic time also prolonged in Group LN. Levobupivacaine with nalbuphine provided more prolonged analgesia (316.13±15.62 mins) which is in accordance with our study.

Jaideep singh et al performed a study among 60 patients posted for lower abdominal surgeries. Group B received intra thecal 0.5% bupivacaine 3ml with fentanyl 25 microgram and group N received intra thecal 0.5% bupivacaine with nalbuphine 0.8mg.They observed that the mean duration of analgesia with fentanyl group was 155.83 min and nalbuphine group was 166.33 min and the mean effective analgesic time was 222.5min for fentanyl group and 231.5 min in nalbuphine group.From this study ,they concluded that

0.8mg nalbuphine as an adjuvant to intrathecal bupivacaine prolongs the duration of postoperative analgesia with lesser side effects .In our study ,we used 0.5mg nalbuphine added to intrathecal levobupivacaine which produced similar effects

In 2013, Misirlioglu k, et al performed a randomized study among 72 patients undergoing elective cesarean section. Group L received intrathecal 0.5% levobupivacaine and fentanyl 25microgram. Group B received intrathecal 0.5% bupivacaine with fentanyl 25microgram. They found that the quality of sensory blockade was equal in both the groups, but group B had complete motor blockade at the beginning and end of the surgery. Hemodynamic and neonatal parameters were similar in both groups. Pruritis - a common side effect in both the groups. They concluded that levobupivacaine with fentanyl has effective sensory blockade with lesser motor blockade but similar hemodynamics than bupivacaine with fentanyl.

In1998,Fournier et al. compared the postoperative pain relief between intrathecal nalbuphine400 µg and intrathecal morphine 160 mcg in 24 geriatric patients undergoing total hip replacement using continuous spinal anesthesia. They observed that intrathecal nalbuphine produces earlier onset of sensory and motor block but the duration of analgesia is shorter than intrathecal morphine group.

This prospective randomized double blinded study was done among 60 patients.

The postoperative analgesic requirements and spinal anaesthesia mediated analgesic effects of levobupivacaine with opioid adjuvants (nalbuphine and fentanyl) was observed in this study.

It showed no statistical significance among patient's Age, Weight, Height, American Society of Anaesthesiologist Physical Status and duration of surgery. The mean age in fentanyl group is 52.43 and nalbuphine group is 52.83. The mean weight of fentanyl group is 56.20 and nalbuphine group is 57.90 .The mean height in fentanyl group is 161.83 and nalbuphine group - 161.67.

Regarding the onset of sensory blockade at T10 level,it was similar in both the groups with p value 0.665 which shows no statistical significance

With regard to the onset of sensory blockade , 26 persons in the fentanyl group attained T6 level in 5mins when compared to nalbuphine group 23 persons attained T6 level in the same time, but it was not statistically significant.

Regarding the onset of motor blockade,L1 level was achieved at 1 min by both the groups. The onset of complete motor blockade at 5 mins is achieved by 26(86.7%) patients in fentanyl group and 15(50.0%) patients in nalbuphine group which is statistically not significant with p value 0.056. So

the onset of complete motor block was more rapid with fentanyl than nalbuphine and this may be explained by the higher lipid solubility & rapid tissue uptake of fentanyl more than nalbuphine.

Also this study shows no significance in duration of motor blockade and two segment regression time between fentanyl and nalbuphine. The mean two segment regression time for fentanyl group is 122.47 ±1.79and for nalbuphine is 123.53± 1.79

According to the hemodynamic parameters, the fentanyl group developed both decrease in systolic and diastolic blood pressures than nalbuphine .

Also in this present study, no statistical significance was observed between fentanyl and nalbuphine groups as regards heart rate, respiratory rate and peripheral oxygen saturation. There was neither bradycardia nor decrease in oxygen saturation was recorded.

As regards the side effects, they were lesser in nalbuphine group than fentanyl group with no statistical significance.8 persons in fentanyl group had hypotension and in nalbuphine group 6 persons had hypotension and its p value is 0.542 which is statistically not significant.

In fentanyl group 3(10%) patients had nausea and vomiting as side effect but in nalbuphine group only one patient has this side effect .It has no statistical significance with p value 0.313(>0.05). Pruritis was noted with

fentanyl group , not in nalbuphine group but it is statistically not significant. shivering was more in fentanyl(6.66%) than nalbuphine group(3.33%) but its not statistically significant.

The duration of analgesia and effective analgesic time was prolonged in nalbuphine group (166.13±6.52) than fentanyl group (160.67± 4.85).The rescue analgesia was given when the VAS score more than or equal to 4.

SUMMARY

SUMMARY

This is a prospective, randomized double blinded study conducted among 60 patients who were posted under elective lower abdominal gynaceological surgery

They were equally divided into

Group A: They received intrathecal fentanyl 25microgram with 0.5% levobupivacaine

Group B: They received intrathecal nalbuphine 0.5mg with 0.5% levobupivacaine.

The onset of sensory and motor block, two segment regression time and the duration of analgesia were analysed. Also hemodynamic parameters and side effects were observed. This study concluded that there is no significance in difference between nalbuphine and fentanyl when combined with levobupivacaine for spinal anaesthesia.

They provide rapid onset of anaesthesia and prolonged duration of analgesia with better hemodynamic stability and lesser side effects.

CONCLUSION

CONCLUSION

We conclude that both Intrathecal nalbuphine and intrathecal fentanyl added to levobupivacaine in spinal anaesthesia improves intraoperative analgesia and prolongs the early postoperative analgesia. There was no increase in the risk of side effects with either of the additives and both groups give similar hemodynamic stability .

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ANNEXURES

ANNEXURE

PROFORMA

DATE:

NAME: AGE:

DIAGNOSIS:

IP NO:

SURGICAL PROCEDURE DONE:

Ht: BMI:

Wt:

PRE OP ASSESSMENT:

HISTORY:

AnyCo-morbid illness

H/O previous surgeries

GENERAL EXAMINATION:

SYSTEMIC EXAMINATION

CVS: RS: P/A: CNS:

AIRWAY EXAMINATION

MMS- DENTITION TMD IID

INVESTIGATIONS

ASA PS CLASSIFICATION:

MEASURES OF STUDY OUTCOME:

INTRA THECAL INJECTION :

COMPLICATIONS IN INTRA OPERATIVE PERIOD:

DURATION OF SURGERY

INTRA OPERATIVE

Time	Sensory block (pain prick)	Motor blockade (bromage scale)	VAS
30 sec			
1min			
2min			
3min			
4min			
5min			
6min			
7min			

INTRA OPERATIVE HEMODYNAMICS:

Events	Time	SystolicBP MmHg	DiastolicBP mmHg	MAP	Heart rate Beats/min	Spo2	complications
Baseline							
During procedure							
Incision							
End of Surgery							

POST OPERATIVE

TIME	0	1	2	3	4	6
VAS						
HR						
SBP						
DBP						
MAP						
RR						
Rescue						
Complications						
Effective						

INFORMATION TO PARTICIPENTS

Investigator : Dr.A.SUGANYA

Name of the Participant:

Title : "COMPARISON OF POSTOPERATIVE ANALGESIA AFTER INTRATHECAL NALBUPHINE WITH LEVOBUPIVACAINE AND INTRATHECAL FENTANYL WITH LEVOBUPIVACAINE AFTER GYNAECOLOGICAL SURGERY"

.(A Prospective,randomized,double blinded study)

You are invited to take part in this research study. We have got approval from the IEC. You are asked to participate because you satisfy the eligibility criteria. We want to compare and study the safety and analgesic efficacy of intrathecal nalbuphine with levo bupivacaine and fentanyl with levobupivacaine

What is the Purpose of the Research:

For gynecological surgeries, efficacy of intrathecal nalbuphine with bupivacaine and fentanyl with bupivacaine

A. Assessment of onset of sensory and motor blockade

B. To assess intra Operative and postoperative hemodynamics
C. To evaluate the effective analgesic time

D. To evaluate the severity of pain using visual analogue scale
E. Complication rate

The Study Design:

All the patients in the study will be divided into two groups.

Group I -intrathecal fentanyl 0.5ml(0.25 microgram) with 0.5% levobupivacaine 3ml

GroupII - intra thecal nalbuphine 0.5ml(0.5mg) with 0.5%levobupivacaine 3ml

Benefits

Intrathgecal nalbuphine reduces post operative opoid consumption and its complications, with minimal side effects and superior pain relief without affecting hemodynamics.

Discomforts and risks

Intravascular local anaesthetic injection

Local anaesthetic toxicity

This intervention has been shown to be well tolerated as shown by previous studies.And if you donot want to participate you will have alternative standard treatment and your safety is our prime concern.

Time:

Date:

Place:

Signature/Thumb Impression of Patient Signature of the Investigator :

Patient Name: Name of the Investigator:

PATIENT CONSENT FORM

Study title: "COMPARISON OF POSTOPERATIVE ANALGESIA AFTER INTRATHECAL NALBUPHINE WITH LEVOBUPIVACAINE AND INTRATHECAL FENTANYL WITH LEVOBUPIVACAINE AFTER GYNAECOLOGICAL SURGERY".(A Prospective, randomized, double blinded study)

Study Center: INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE, RAJIV GANDHI GOVT.GENERAL HOSPITAL, MADRAS MEDICAL COLLEGE, CHENNAI-03

Participant Name: Age: Sex: I.P.No:

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the procedure. I have been explained about the safety, advantage and disadvantage of the technique.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it ,even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

Time:

Date:

Place:

Signature of the investigator: Signature/thumb impression of patient

Name of the investigator: Patient name:

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராயச்சியின் தலைப்பு

தண்டுவட உறையுள் லிவோபுபிவெகேன் உடன் நால்புபின் மற்றும் லிவோபுபிவெகேன் உடன் பென்டனைல் செலுத்தி மகளிர் மருத்துவ அறுவை சிகிச்சைக்குப் பின் வலி நிவாரணத் தன்மையை ஒப்பிடல்.

ஆய்வு நிலையம் : மயக்கவியல் துறை, சென்னை மருத்துவக் கல்லூரி சென்னை - 3.

பங்கு பெறுவரின் பெயர் :

பங்குபெறுபவரின் எண் :

பங்குபெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக்கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கின்றேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் 'இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிகிறேன். ☐

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம்..... தேதி.....

ஆய்வாளரின் பெயர் .....

ஆராய்ச்சி தகவல் தாள்

ஆராய்ச்சி தலைப்பு

தண்டுவட உறையுள் லிவோபுபிவெகேன் உடன் நால்புபின் மற்றும் லிவோபுபிவெகேன் உடன் பென்டனைல் செலுத்தி மகளிர் மருத்துவ அறுவை சிகிச்சைக்குப் பின் வலி நிவாரணத் தன்மையை ஒப்பிடல்.

ஆராய்ச்சியாளர் பெயர் : மருத்துவர்.அ.சுகன்யா

பங்கேற்பாளர் பெயர் :

ஆராய்ச்சியின் நோக்கம்

தண்டுவட உறையுள் லிவோபுபிவெகேன் உடன் நால்புபின் மற்றும் லிவோபுபிவெகேன் உடன் பென்டனைல் செலுத்தி மகளிர் மருத்துவ அறுவை சிகிச்சைக்குப் பின் வலி நிவாரணத் தன்மையை ஒப்பிடல்.

1. மரத்துப் போகும் தன்மையின் ஆரம்ப நேர நிலை கண்டறிதல்
2. அறுவை சிகிச்சையின்போதும், அதன் பின்பும், நாடித்துடிப்பு, இரத்த அழுத்தம்.
3. அறுவை சிகிச்சையின்போது இதர வலி நிவாரணிகளின் தேவை
4. பக்க விளைவுகள்
5. அறுவை சிகிச்சைக்கு பின்னான விசுவல் அனலாக் அளவுகோலின் படி வலியின் அளவு.

ஆய்வு முறை

ஆய்வில் பங்குபெறும் நோயாளிகள் இரண்டு குழுக்களாகப் பிரிக்கப்படுவர்.

குழு-1 தண்டுவட உறையுள் லிவோபுபிவெகேன் உடன் பென்டனைல் செலுத்துதல்

குழு-2 தண்டுவட உறையுள் லிவோபுபிவெகேன் உடன் நால்புபின் செலுத்துதல்

நன்மைகள்

1) அறுவை சிகிச்சைக்குப் பின்னர் வலி நிவாரணத்தின் தன்மை நீட்டிக்கப்படுகின்றது.

2) இதர வலி நிவாரணிகளின் தேவை வெகுவாக குறைக்கப்படுகின்றன.

பக்கவிளைவுகள்

ஊசி போடும்போது அசௌகரியம் ஏற்படலாம். மரத்துப்போகும் ஊசியின் மூலம் இது தவிர்க்கப்படும். குறைந்த இரத்த அழுத்தம், குறைந்த நாடித்துடிப்பு ஏற்படலாம். அதற்கு மாற்று மருந்துகள் உடனடியாக கொடுக்கப்படும்.

இந்த முறையான ஆய்வு ஏற்கனவே பல இடங்களில் நடத்தப்பட்டுள்ளது. மேலும் இதன் பாதுகாப்பு உறுதிசெய்யப்பட்டுள்ளது. நீங்கள் இந்த ஆய்வில் பங்குகொள்ள விரும்பவில்லை என்றால் எப்போதும் உபயோகிக்கப்படும் மருந்தே கொடுக்கப்படும். உங்கள் பாதுகாப்பே எங்களின் முக்கிய நோக்கம்.

இந்த ஆய்வு சம்பந்தமான எல்லா புள்ளி விவரங்கள் மற்றும் நோயாளிகளின் விவரங்கள் ரகசியமாக வைக்கப்படும். இந்த ஆய்வு சம்பந்தப்பட்ட எல்லா பரிசோதனைகள், மருந்துகள் மற்றும் மருத்துவ சேவைகள் அனைத்தும் நோயாளிகளுக்கு இலவசமாக வழங்கப்படும்.

ஆய்வாளரின் பெயர் **பங்குபெறுபவரின் பெயர்**

ஆய்வாளரின் கையொப்பம் **பங்குபெறுபவரின் கையொப்பம்**

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To

Dr.A.Suganya
I Year PG in MD Anaesthesiology
Department of Anesthesiology & Critical Care
Madras Medical College
Chennai 600 003

Dear Dr.A.Suganya,

The Institutional Ethics Committee has considered your request and approved your study titled **"COMPARISON OF POST-OPERATIVE ANALGESIA AFTER INTRATHECAL NALBUPHINE WITH LEVOBUPIVACAINE AND INTRATHECAL FENTANYL WITH LEVOBUPIVACAINE AFTER GYNACOLOGICAL SURGERY " - NO.23062017(A)**

The following members of Ethics Committee were present in the meeting hold on **20.06.2017** conducted at Madras Medical College, Chennai 3

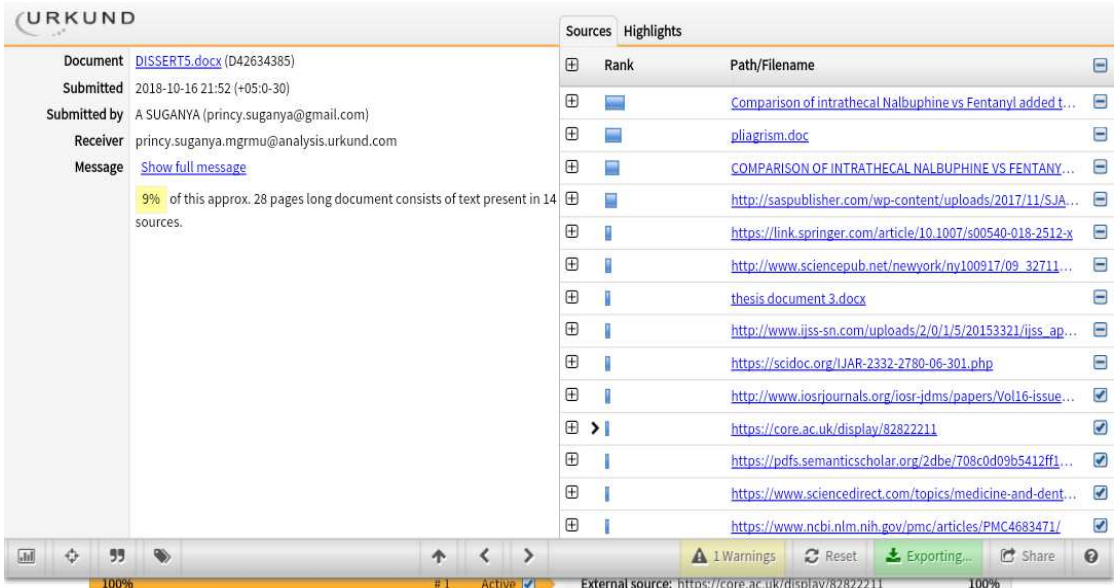
1. Prof.Dr.C.Rajendran, MD., :Chairperson
2. Prof.R.Narayana Babu,MD.,DCH., MMC,Ch-3 : Deputy Chairperson
3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3 :Member Secretary
4. Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3 : Member
5. Prof.A.Pandiya Raj,Director, Inst. of Gen.Surgery,MMC : Member
6. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai : Member
7. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3 : Member
8. Thiru S.Govindasamy, BA.,BL,High Court,Chennai : Lawyer
9. Tmt.Arnold Saulina, MA.,MSW., :Social Scientist
10. Tmt.J.Rajalakshmi, JAO,MMC, Ch-3 : Lay Person

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary – Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003



and adverse effects.post operatively visual analogue scale score was used to asses the pain .The effective analgesic time was noted.The patients with pain score <3 received rescue analgesia Injection paracetamol 1000mg i.v.the time for the first rescue analgesia was longer in nalbuphine group but the difference was insignificant.adverse effects were less common in nalbuphine group than fentanyl group but the difference was insignificant. They also observed that there was nil significance between the two groups with respect to intra operative and post operative hemodynamic variables.

• GANGANDEEP SINGH et al They did a study on 80 pregnant women posted for elective cesarean section who were divided into group A for them intrathecal 0.5%levobupivacaine with fentanyl 25microgram given and group B for them intrathecal 0.5% levobupivacaine given. They evaluvated the time of onset of sensory blockade,time to complete sensory blockade and two segment regression time,time for rescue analgesia and hemodynamics were monitored.they observed that the combination of fentanyl with levobupivacaine has achieved earlier complete sensory and motor blockade than levobupivacaine alone group.Also levobupivacaine with fentanyl reduced the need of postoperative analgesics.

• MUKHERJEE et al They did a study on 100 patients undergoing elective lower limb orthopaedic surgery under subarachnoid block.They used different doses of intrathecal nalbuphine (200,400,800 micrograms) added to 0.5% hyperbaric bupivacaine for Group A,B,and C respectively.They assessed the onset time for sensory and complete motor blockade and effective analgesic time,2 segment regression time and hemodynamics of the patients.

they concluded that the duration of sensory block and effective analgesia were prolonged with

doses of 400microgram (group B)and 800micrograms(group C) of nalbuphine with bupivacaine but higher doses of nalbuphine produced higher side effects

• MISIRLIOGLU et al They did a study among 72 patients undergoing elective cesarean section .group L received intrathecal 0.5% levobupivacaine and fentanyl 25microgram .group B received intrathecal 0.5% bupivacaine with fentanyl 25microgram.they assessed the time to achieve sensory block upto T6,time to S2 regression,sensory and motor blockades at the end of the surgery .hemodynamic parameters like heart rate,SBP,DBP,neonatal APGAR score were recorded.they found that the quality of sensory blockade was equal in both the groups,but group B had complete motor blockade at the beginning and end of the surgery.Hemodynamic and neonatal parameters were similar in both groups.pruritis was a common side effect in both groups.they concluded that levobupivacaine with fentanyl has effective sensory blockade with less motor blockade and similar hemodynamics than bupivacaine with fentanyl.

• JAIDEEP SINGH et al They did a study in 60 patients posted for lower

URKUND

Urkund Analysis Result

Analysed Document: DISSERT5.docx (D42634385)
Submitted: 10/16/2018 6:22:00 PM
Submitted By: princy.suganya@gmail.com
Significance: 9 %

Sources included in the report:

pliagrism.doc (D42387640)
Comparison of intrathecal Nalbuphine vs Fentanyl added to 0.5% hyperbaric bupivacaine for perioperative anaesthesia and perioperative post operative analgesia in Hernioplasty.docx (D42330323)
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45

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled "**COMPARISON OF POSTOPERATIVE ANALGESIA AFTER INTRATHECAL NALBUPHINE WITH LEVOBUPIVACAINE AND FENTANYL WITH LEVOBUPIVACAINE AFTER GYNAECOLOGICAL SURGERY"** of the candidate **Dr.A.SUGANYA** with registration number 201620016 for the award of **M.D** in the branch of **ANAESTHESIOLOGY**. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion and the results shows 9% of plagiarism in the dissertation.

Prof.Dr.B.CHANDRIKA.M.D.D.A,
PROFESSOR OF ANAESTHESIOLOGY,
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ABBREVIATIONS

WT	-	weight
HT	-	height
ASA PS	-	American Society of Anaesthesiologist Physical Statusbn
DS	-	Duration of surgery
2SRT	-	2 segment regression time
DMB	-	duration of motor blockade
HR	-	heart rate
SBP	-	systolic blood pressure
DBP	-	diastolic blood pressure
MAP	-	mean arterial pressure
RR	-	respiratory rate
DA	-	duration of analgesia
VAS	-	visual analog scale
H	-	hypotension
S	-	shivering
NV	-	nausea and vomiting
P	-	pruritis

GROUP A S NO	AGE	WT (KG)	HT (CM)	ASA PS	DS (min)	ONSET SENSORY BLOCK 30SEC	1MIN	2MIN	3MIN	4MIN	5MIN	6MIN	7MIN	ONSET OF MOTOR BLOCK 30SEC	1MIN	2MIN	3MIN	4MIN	5MIN	6MIN	7MIN	2SRT OF SB (min)	DMB (min)	BL	DP	INCISION
1	45	60	163	1	105	0	T12	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T7	T6	118	140	113	106	100
2	44	60	157	1	100	0	T12	T10	T10	T8	T5	T5	T5	0	L1	T12	T12	T10	T7	T7	T6	117	139	115	105	99
3	46	64	158	2	105	0	T11	T10	T10	T8	T5	T5	T5	0	L1	T12	T12	T10	T7	T7	T6	120	144	110	108	97
4	42	62	155	1	110	0	T11	T10	T10	T8	T5	T5	T5	0	L1	T12	T12	T10	T7	T7	T6	125	145	118	103	96
5	50	58	153	2	100	0	T12	T10	T10	T8	T5	T6	T5	0	L1	T12	T12	T10	T7	T8	T6	122	130	116	109	99
6	55	57	155	1	95	0	T12	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T7	T6	123	144	110	110	98
7	60	56	156	2	105	0	T12	T10	T10	T8	T6	T6	T5	0	L1	T12	T12	T10	T8	T8	T6	121	140	114	111	96
8	52	55	155	1	110	0	T12	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T7	T6	122	139	116	112	98
9	51	62	159	1	108	0	T11	T10	T10	T8	T5	T6	T5	0	L1	T12	T12	T10	T7	T8	T6	126	139	112	105	99
10	53	61	155	1	90	0	T11	T10	T10	T8	T5	T5	T5	0	L1	T12	T12	T10	T7	T7	T6	124	144	120	115	95
11	44	59	169	1	96	0	T12	T10	T10	T8	T5	T5	T5	0	L1	T12	T12	T10	T7	T7	T6	118	141	121	110	100
12	48	58	166	1	98	0	T12	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T7	T6	119	140	115	115	99
13	59	60	163	2	102	0	T11	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T7	T6	118	142	113	112	98
14	57	52	162	2	110	0	T12	T10	T8	T8	T5	T5	T5	0	L1	T12	T10	T10	T7	T7	T6	120	144	119	117	97
15	60	55	166	2	106	0	T12	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T7	T6	126	145	117	119	98
16	53	59	165	1	115	0	T12	T11	T10	T8	T6	T5	T5	0	L1	L1	T12	T10	T8	T7	T6	125	142	111	106	99
17	51	57	170	1	97	0	T12	T10	T10	T8	T5	T5	T5	0	L1	T12	T12	T10	T7	T7	T6	125	143	112	104	98
18	52	58	155	2	112	0	T12	T10	T10	T8	T5	T5	T5	0	L1	T12	T12	T10	T7	T7	T6	123	144	118	108	100
19	49	52	157	1	90	0	T12	T10	T8	T6	T5	T5	T5	0	L1	T12	T10	T8	T7	T7	T6	125	142	119	107	93
20	48	53	159	1	110	0	T12	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T7	T6	122	138	120	110	97
21	57	50	155	1	115	0	T12	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T7	T6	118	139	121	120	99
22	62	51	159	2	106	0	T12	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T7	T6	119	140	110	116	95
23	53	53	168	2	98	0	T12	T10	T10	T8	T5	T5	T5	0	L1	T12	T12	T10	T7	T7	T6	125	141	117	119	100
24	52	54	167	1	100	0	T12	T11	T10	T8	T5	T5	T5	0	L1	L1	T12	T10	T7	T7	T6	122	144	118	113	98
25	48	56	171	1	95	0	T12	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T8	T6	118	145	119	110	99
26	57	55	170	1	105	0	T12	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T8	T6	126	142	113	105	95
27	59	50	165	2	90	0	T12	T10	T10	T8	T6	T5	T5	0	L1	T12	T12	T10	T8	T7	T6	122	143	111	107	99
28	61	52	166	2	95	0	T11	T11	T10	T8	T6	T5	T5	0	L1	L1	T12	T10	T8	T7	T6	119	140	112	110	99
29	50	51	170	1	100	0	T12	T10	T8	T6	T5	T6	T5	0	L1	T12	T10	T8	T7	T7	T6	118	142	118	109	100
30	55	56	166	1	94	0	T11	T10	T8	T6	T5	T5	T5	0	L1	T12	T10	T8	T7	T7	T6	120	125	120	115	98

PERIOPERATIVE SYSTOLIC BP										PERIOPERATIVE DIASTOLIC BP										PERIOPERATIVE MAP						
ES	0HR	1HR	2HR	3HR	4HR	6HR	BL	DP	INCISION	ES	0HR	1HR	2HR	3HR	4HR	6HR	BL	DP	INCISION	ES	0HR	1HR	2HR	3HR	4HR	6HR
121	124	124	120	120	122	110	70	70	60	70	70	80	82	83	80	88	84.33	82	73.33	87	88	94.67	94.67	95.33	94	95.33
120	122	126	119	119	120	115	71	72	58	72	71	81	83	85	86	70	85.67	83	71.67	88	88	96	95	96.33	97.33	83.33
125	127	125	118	118	122	110	68	70	59	74	70	78	80	79	84	89	82	82.67	71.67	91	89	93.67	94.67	92	96.67	96
100	89	110	113	112	115	116	69	70	61	66	59	79	79	80	83	85	85.33	81	77.33	77.33	69	89.33	90.33	90.67	93.67	95.33
130	130	127	125	124	120	114	72	72	62	72	74	76	80	81	80	86	87.33	84.33	74.33	91.33	92.67	93	95	95.33	93.33	95.33
119	126	128	124	125	118	116	73	74	59	70	72	78	81	80	83	82	85.33	86	72	86.33	90	94.67	92	95	94.67	93.33
102	90	108	110	120	119	112	77	76	58	74	60	79	80	80	84	83	89.33	87.67	70.67	83.33	70	88.67	90	93.33	95.67	93.67
130	126	132	128	128	123	115	75	77	60	72	71	80	81	80	85	80	88.67	84	80.67	91.33	89.33	97.33	96.67	96	96.33	93
128	128	130	126	126	119	119	66	70	61	70	70	81	80	80	83	83	81.33	81.67	73.67	89.33	89.33	97.33	95.33	95.33	95	95
102	90	112	116	113	120	108	69	70	58	59	60	69	63	66	70	74	86	85	70.33	73.33	70	78	80.67	81.67	86.67	85.33
123	125	128	121	121	122	120	63	70	60	70	72	79	81	82	79	82	82.63	83.33	73.33	87.67	89.67	95.33	94.33	95	93.33	94.67
122	130	129	120	120	122	118	64	69	58	69	74	78	80	80	84	89	81	84.33	71.67	86.67	92.67	95	93.33	93.33	96.67	98.67
120	124	127	127	126	128	115	69	71	59	69	77	79	81	84	79	83	83.67	84.67	72	86	92.67	95	96.33	98	95.33	93.67
127	128	126	126	127	125	117	70	70	57	70	70	80	80	83	80	85	86.33	85.67	70.33	89	89.33	95.33	95.33	97.67	95	95.67
126	125	129	122	123	127	111	72	73	61	71	71	81	80	82	83	81	87	88.33	73.33	89.33	89	97	92	95.67	97.67	91
125	127	127	122	122	127	112	71	71	60	71	74	80	82	81	80	80	84.33	82.67	73	87.67	91.67	95.67	95.33	94.67	95.67	90.67
101	90	105	108	110	113	114	73	65	58	59	60	63	66	70	72	75	86	77.33	71.33	73	70	77	80	83.33	85.67	97
129	125	127	120	121	120	118	77	77	59	69	72	80	80	86	85	83	90.67	87.33	72.67	89	89.67	95.67	93.33	97.67	96.67	93.67
100	90	97	110	108	110	115	75	73	58	60	59	60	66	68	70	71	89.67	84.33	69.67	73.33	71	72.33	80.67	81.33	83.33	85.67
126	124	122	121	126	118	113	79	75	57	73	70	78	82	82	80	87	92.67	86.67	70.33	90.67	88	92.67	95	96.67	92.67	95.67
124	125	124	121	123	128	111	70	75	60	70	75	77	80	80	82	86	87	90	73	87	91.67	92.67	93.67	94.33	97.33	94.33
100	89	98	103	109	110	120	71	71	56	58	60	66	65	68	68	69	84	86	69	72	69.67	76.67	77.67	81.67	82	86
128	130	125	125	123	121	110	72	72	60	70	72	80	79	79	85	84	87	87.67	73.33	89.33	91.33	90	94.33	93.67	97	92.67
125	127	127	120	124	120	109	77	73	62	71	71	81	80	79	88	88	90.67	86.33	74	89	89.67	96.33	93.33	92	98.67	92
127	128	126	123	122	122	108	73	73	63	72	76	82	84	80	80	84	88.33	85.33	75	90.33	93.33	96.66	97	94	94	92
102	90	100	103	107	110	110	74	75	60	61	60	60	65	63	61	62	87	85	71.67	74.67	70	73.33	77.67	77.67	77.33	78
130	129	127	125	128	125	112	75	75	59	70	75	80	80	80	83	82	87	85.67	72.33	90	93	95.67	95	96	97	92
127	128	127	124	124	127	115	79	79	58	71	74	80	81	82	84	83	90	89.33	71.67	89.67	92	95.67	95.35	96	98.33	93.67
107	90	126	127	130	120	120	72	78	59	66	60	81	82	80	81	85	87.33	88.33	72.67	79.67	70	96	97	96.67	93.33	96.67
121	130	129	122	125	126	121	73	75	60	71	72	79	80	83	80	86	88.67	88.33	72.67	87.67	91.33	95.67	94	97	95.33	97

PERIOPERATIVE HR									PERIOPERATIVE SPO2 %									POSTOPERATIVE RR (MIN)						
BL	DP	INCISION	ES	0HR	1HR	2HR	3HR	4HR	6HR	BL	DP	INCISION	ES	0HR	1HR	2HR	3HR	4HR	6HR	0HR	1HR	2HR	3HR	4HR	6HR
90	90	90	90	90	90	90	90	90	90	99	98	100	100	100	100	99	99	99	99	12	12	12	12	12	12
88	89	79	77	81	90	91	92	84	82	99	98	100	100	100	100	100	100	99	99	12	12	12	12	12	12
85	87	80	76	82	93	92	90	85	83	98	98	100	100	100	100	98	99	99	99	13	13	13	13	13	13
83	88	80	77	80	90	90	91	84	81	99	98	100	100	100	100	99	99	99	98	14	14	14	14	14	14
84	85	81	78	80	94	89	90	88	80	98	98	100	100	100	100	99	99	99	99	12	12	12	12	12	12
89	86	78	77	82	93	93	90	84	79	99	98	100	100	100	100	98	99	99	99	14	14	14	14	14	14
85	88	79	76	83	90	91	92	85	78	99	98	100	100	100	100	100	100	99	99	12	12	12	12	12	12
85	84	80	79	84	90	92	89	82	80	98	99	100	100	100	100	99	99	98	99	14	14	14	14	14	14
88	84	80	78	85	91	90	88	84	79	98	99	100	100	100	100	100	100	99	99	13	13	13	13	13	13
90	89	81	75	80	92	90	91	89	80	98	98	100	100	100	100	99	99	99	99	12	12	12	12	12	12
89	88	82	86	81	91	91	90	90	79	98	98	100	100	100	100	99	98	98	98	14	14	14	14	14	14
85	84	80	80	79	90	92	88	89	81	98	99	100	100	100	100	100	99	99	98	12	12	12	12	12	12
86	84	81	81	78	91	94	89	89	80	98	99	100	100	100	100	100	100	99	99	14	14	14	14	14	14
89	88	82	82	80	90	90	91	87	82	98	98	100	100	100	100	99	98	99	98	12	12	12	12	12	12
88	86	83	80	85	92	91	90	80	83	98	98	100	100	100	100	100	99	99	99	12	12	12	12	12	12
87	89	80	84	88	90	92	95	85	79	98	98	100	100	100	100	100	100	99	99	14	14	14	14	14	14
84	90	79	85	82	92	90	94	89	78	98	98	100	100	100	100	100	99	98	98	13	13	12	12	12	12
85	91	80	87	80	90	91	92	85	90	99	99	100	100	100	100	100	100	99	99	14	14	14	14	14	14
80	90	79	82	82	91	90	90	86	79	99	99	100	100	100	100	100	100	99	98	13	13	12	12	12	12
90	90	78	80	84	90	91	92	87	82	99	99	100	100	100	100	99	99	99	99	14	14	14	14	14	14
91	88	79	83	79	92	92	90	80	83	99	99	100	100	100	99	99	98	99	98	12	12	12	12	12	12
83	89	80	84	78	91	90	91	83	81	98	98	100	100	100	100	99	99	99	99	13	13	13	13	13	13
86	83	81	79	79	90	90	90	84	79	98	98	99	100	100	100	100	100	99	99	13	13	13	13	13	13
89	84	80	77	80	94	92	92	81	77	99	98	100	99	100	100	100	99	99	98	12	12	12	12	12	12
87	88	82	77	81	95	93	92	83	81	99	99	100	100	100	100	100	100	99	99	14	14	14	14	14	14
88	87	83	79	84	94	90	91	80	80	98	98	100	100	100	100	100	100	99	98	12	12	12	12	12	12
82	89	79	80	82	92	94	93	83	82	97	98	99	100	100	100	99	99	99	98	12	12	12	12	12	12
85	80	80	81	84	91	95	92	84	80	98	98	100	100	100	100	100	99	99	98	12	12	12	12	12	12
83	89	80	79	80	90	93	91	87	82	99	99	98	99	99	99	98	98	99	98	12	12	12	12	12	12
80	87	83	80	81	90	94	90	86	81	99	99	100	100	100	100	100	100	99	99	12	12	12	12	12	12

VAS						RESCUE ANALGESIA						POSTOP COMPLICATIONS						DA
0HR	1HR	2HR	3HR	4HR	6HR	0HR	1HR	2HR	3HR	4HR	6HR	0HR	1HR	2HR	3HR	4HR	6HR	(MIN)
0	1	2	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	P	NIL	NIL	NIL	NIL	NIL	160
0	2	3	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	176
0	1	3	4	3	2	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	164
0	2	3	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	H	NIL	NIL	NIL	NIL	NIL	166
0	2	4	3	3	3	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	154
0	1	2	3	4	2	NIL	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	173
0	2	3	4	3	2	NIL	NIL	NIL	NEEDED	NIL	NIL	H	NIL	NIL	NIL	NIL	NIL	168
0	2	3	4	3	2	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	168
0	2	3	4	3	2	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	156
0	1	2	4	3	2	NIL	NIL	NIL	NEEDED	NIL	NIL	H	NIL	NIL	NIL	NIL	NIL	158
0	2	3	4	3	2	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	160
0	1	2	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	S	NIL	NIL	NIL	NIL	NIL	163
0	1	2	3	4	3	NIL	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	164
0	2	3	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	170
0	1	2	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	168
0	1	2	4	3	2	NIL	NIL	NIL	NEEDED	NIL	NIL	S	NIL	NIL	NIL	NIL	NIL	156
0	1	2	4	2	2	NIL	NIL	NIL	NEEDED	NIL	NIL	H	NIL	NIL	NIL	NIL	NIL	173
0	2	3	4	2	2	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	165
0	2	3	4	2	3	NIL	NIL	NIL	NEEDED	NIL	NIL	H	NIL	NIL	NIL	NIL	NIL	165
0	1	2	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	170
0	1	2	3	4	3	NIL	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	173
0	1	2	4	3	2	NIL	NIL	NIL	NEEDED	NIL	NIL	H	NIL	NIL	NIL	NIL	NIL	166
0	2	3	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	165
0	2	3	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	170
0	1	2	3	4	2	NIL	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	173
0	1	2	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	H	NIL	NIL	NIL	NIL	NIL	166
0	1	2	4	3	2	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	164
0	1	2	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	165
0	1	2	4	3	2	NIL	NIL	NIL	NEEDED	NIL	NIL	H	NIL	NIL	NIL	NIL	NIL	164
0	1	2	4	3	3	NIL	NIL	NIL	NEEDED	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	170